THE SKINNY OLD CAT: PROBLEM OR NORMAL?
The ART OF AGING GRACEFULLY
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Feline life expectancy has risen, on average, to 14-16 years of age. This increase is likely a result of compliance with vaccination protocols, nutritional counselling/the availability of nutritionally balanced feline-specific diets, and improved dental hygiene. A” senior” cat is one 11-14 years (Pittari) of age, “geriatric” referring to cats 15+ years: these age ranges correlate roughly with human ages of 60-72 and 76+, respectively.1

A cat may begin to manifest serious age-related disorders, (e.g. renal insufficiency) on average, around 8 - 9 years of age. This does NOT make that individual old..., or less treatable. With aging comes a set of cellular changes that are somewhat predictable and which need to be taken into consideration in our approach to health care, both preventative as well as therapeutic. At any age there are changes and disorders, particular to that age group or stage of progression.

To paraphrase Robbins2, the complex process of aging begins at the moment of conception, involves differentiation and maturation and, at some point, leads to the progressive loss of functional capacity characteristic of senescence ending in death. This occurs at an organismal level as well as at a cellular level. The former may be affected by genetics, social environment, nutrition, and the occurrence of age-related diseases. Cellular aging, on the other hand, includes progressive accumulation of sub-lethal injury (e.g., from free radical damage), resulting in either cell death or diminished capacity of the cell to repair itself. We can impact these changes to some degree through nutritional (and other) intervention.

Nutritional considerations of aging
Maintenance energy requirements (MER) vary with age, genetic potential, health status, and gender (intact or altered). As humans, dogs, rats and cats (until ~ age 11) age, their MER decrease. From age 12 onwards, cats are different and their MER increases.3-5 As a consequence, cats under 12 years tend to become overweight or obese as their energy needs decrease without appropriate limitation in energy intake. Lean body mass (LBM: skeletal muscle, bone, skin and organs) decreases with advancing age.

Studies in geriatric cats 12+ years show that fat digestibility decreases with age.6 Additionally, approximately 20% of cats over 14 years of age have reduced protein digestion.6 This is clinically relevant when we try to design the optimal nutritional regime for our older feline patients: protein and fat restriction may well be contraindicated. Especially if underweight, older cats will benefit from a more energy-dense, highly digestible diet to help offset these age-related digestive and metabolic changes.
Key to determining the appropriate diet for any given individual is a nutritional assessment. This should include determining body weight, body condition, muscle condition and percentage weight change. Using a diet history form is very helpful.

Recent work has studied the effects of feeding the healthy, older cat with dietary antioxidants (Vitamin E, beta carotene) alone or in combination with a prebiotic (chicory root) and a blend of oils to supplement n-3 and n-6 fatty acids and determined that these had a beneficial effect on the health and longevity of cats when compared to a complete and balanced diet. While all cats lost weight as they aged, those in the fully supplemented group lost less weight than those in the other two groups. Other beneficial effects noted were longer life, improved LBM scores, improved fecal microflora, and fewer diseases (notably gastrointestinal) during the study.

Weight loss in older cats can be a frustrating and worrying change. While possibly normal in the older individual, it is of great importance to the cat and the client that the cause be determined. (Figures 1 & 2). Optimising oral and dental health cannot be over-emphasized, yet clients may express concern about anaesthetising the elderly cat. Proper staging of the patient and taking appropriate precautions were found to minimize peri-anaesthetic complications; age was not found to be a risk factor in two studies (Table 1).

The skinny older cat has limited ability to conserve his/her body proteins. Inappetance results in a negative nitrogen balance, protein: calorie malnutrition and deterioration of protective mechanisms impacting immunity, red cell hemoglobin content, muscle mass as well as tissue healing ability. Inappetance and anorexia must be dealt with promptly and adequately. Cats have limited storage of many nutrients and restricted ability to down-regulate numerous metabolic processes. They were designed to eat multiple small meals per day, high in protein, and moderate in fat. Hepatic lipidosis is always a risk, especially in the previously obese cat. It is essential to daily calculate caloric and protein requirements, just as one routinely calculates fluid needs as part of the therapeutic plan. [Calories: 50 kcal/kg ideal BW/day; 5 g protein/kg ideal BW/day]. Appetite stimulants including cyproheptadine (1 mg/cat PO BID), mirtazapine (2-4 mg/cat PO q72h) may help jump-start a cat’s appetite, but one must be wary not to lose sight of total calories consumed. If a cat is eating but not enough, supportive feeding (assisted syringe feeding or tube feeding) should be considered.

For a patient with apparent maldigestion, such as seen with chronic small intestinal disease, folate and cobalamin supplementation has been shown to be beneficial (folate: 0.5-1.0 mg/cat/day PO X 1 month; cobalamin 250 mg/cat SC once weekly X 6 weeks).

Age-associated illnesses
There is a marked increase in metabolic disturbances related to the urinary tract (chronic kidney disease (CKD), pyelonephritis and certain forms of lower urinary tract disorders (LUTD) calcium oxalate ureteronephrolithiasis), endocrine system (hyperthyroidism, diabetes mellitus), arthritis, dental diseases and neoplasia with increasing age. Certain infectious diseases become more likely in the older individual (e.g., FIP). A decline in functioning of the special senses occurs frequently and behaviour changes suggestive of cognitive dysfunction may be seen in some individuals.
Ophthalmologic age-related changes include iris atrophy, melanin deposition on the irises and lenticular sclerosis. While the former do not appear to affect vision, lenticular sclerosis results in a decreased acuity most obvious in dim lighting. Impaired hearing is fairly common in older cats with selective frequencies being affected, similar to that which occurs in older humans. The end-result of these alterations in perception may be “nocturnal yowling” as the individual strives to orient him/herself with the help of cues from the caregiver. Other causes of this behaviour include hyperthyroidism or hypertension (both presumably resulting in agitation), cognitive dysfunction or pain.

Development of inappropriate elimination behaviour may have several age-associated causes. Pain from arthritis may make getting to or getting into the box difficult. Past experiences of discomfort from cystitis or difficult stool passage may result in aversion to use of the litter box. Urge incontinence (urinary or fecal) may result in the inability to get to the box in a timely fashion resulting in the development of an alternative location for eliminative behaviours. Hyperthyroidism may result in defecation of normal or diarrheic feces outside the litter box.

We also see conditions related to altered hydration and nutritional requirements, such as constipation. Constipation is a sign of dehydration. Cellular water content has priority over fecal water content, thus primary treatment should be directed towards rehydration and correction of the underlying cause(s) of that problem, rather than at the consistency of the stool and its movement (e.g. with laxatives). Use of promotility agents, laxatives, osmotic agents and fiber-enriched diets should be used conservatively and concurrently with rehydration.

Because of the reduced ability that most older cats have to reclaim water from their urine, special attention should be paid to counselling the client regarding hydration. Circulating water fountains are accepted by many cats as are flavoured broths. Increasing the proportion of canned food fed and adding water to the food are the easiest ways to address the increased fluid needs of the cat. Subcutaneous fluids administered at home become part of daily maintenance care for many elderly cats.

Normal radiographic changes seen in the older feline patient include an increase in sternal contact of the heart. A decrease in bone density may be seen in very elderly individuals. Some minor calcific changes may occur in the pulmonary parenchyma of normally aging cats. Spondylosis should be looked for especially of the lumbar vertebrae, but bony changes may be seen in any part of the spinal column as well as degenerative, proliferative or lytic changes of the joints. Calcifications may be noted in the kidneys: these are often insignificant, representing calcification of old clots. Differentiation from nephroliths can be made with aid of ultrasound. Similarly, adrenal calcification should not be over-interpreted in cats, as it may be a normal, age-related change.

**With age comes pain**

Oral diseases such as periodontal disease, root exposure, resorptive lesions, stomatitis and oral masses are all painful. Surgical manipulations of tissue result in inflammation as well as direct trauma and cell damage which will initiate the pain response. Similarly, common procedures including blood collection, intravenous catheter placement, restraint of a thin or arthritic patient may be uncomfortable. In addition, there are numerous potentially chronic painful conditions.
Bacterial cystitis and pyelonephritis are more frequent in older cats while the incidence of interstitial/sterile cystitis or inflammatory bowel disease is not different than in cats of younger age groups. The likelihood of neoplasia increases with increasing age. The need for analgesia MUST be considered as part of any treatment plan for the older cat.

Recognition of chronic pain and arthritic pain is a relatively recent event. The incidence of osteoarthritis or degenerative joint disease appears to be much more common that previously thought and is probably a major cause of discomfort in ageing cats. In three studies retrospectively assessing radiographs taken of cats over 12 years of age, or of any age, the prevalence of findings suggestive of DJD was 90%, 22% and 34%, respectively with more older cats showing radiographic changes. Only 4%, 33% and 16.5% had notation of restricted mobility in the medical record indicating that appropriate questions were not being asked of owners, that cats do not experience or that they don’t show discomfort from these joint changes.

A recent study prospectively evaluated cats of all ages to determine the prevalence of radiographic signs of DJD. Most (92%) cats had radiographic evidence of DJD; 91% had at least 1 appendicular site affected and 55% had ≥ 1 site of axial DJD. Affected joints in descending order of frequency were hip, stifle, tarsus, and elbow. The thoracic segment of the spine was more frequently affected than the lumbosacral segment. Grading the severity of each of the radiographic changes identified, they found that for each 1-year increase in cat age, the expected total DJD score increased by an estimated 13.6%. They concluded that radiographically visible DJD is very common in domesticated cats, even in young animals and is strongly associated with age.

Yet lameness is not a common clinical sign of this problem in cats: signs are insidious or attributed to ageing. They include inappropriate elimination (often adjacent to the litter box), decreased grooming, developing antipathy for being combed, reluctance to jump up or down, sleeping more, moving less, withdrawing from human interaction, and possibly even hiding. When activity monitors were attached to cats’ collars, activity counts increased with non-steroidal anti-inflammatory drug (NSAID) treatment suggesting alleviation of musculoskeletal discomfort.

**Caring for the elderly cat**

Older feline patients have particular therapeutic and nursing needs. It is important to restrict the hospital stay to as short as possible, as the older cat is less tolerant of the hospital environment and is more prone to depression. Many conditions require on-going home care, such as subcutaneous (SC) fluid administration, frequent medication administration and dietary manipulation.

Some cats prefer medications administered subcutaneously rather than orally; when the agent exists in SC usable format, this is often an easier route for clients to use. Palatability of diets, especially in the face of declining senses, is especially important. Many older cats need an increase in biologically-available protein rather than a decreased amount. Special thought should be given with each older patient as to the potential need for analgesia. Slow, gentle persistence with acute and empathic observation are our best tools in the care and handling of older cats.
A screening program for the older cat is an excellent management tool. The author’s older cat program consists of a comprehensive examination, urinalysis, blood pressure determination and a blood panel consisting of a CBC with differential, biochemical screen including a basal serum T4, amylase, lipase and electrolytes. This is recommended annually for cats 8-13 years and twice annually after 14 years of age or once abnormalities have been detected.

Along with the ability to help and prolong life, comes the responsibility to ensure quality of life. “Just because we can, doesn’t mean we should.” The author refers the reader to a paper on the Ethical Issues in Geriatric Feline Medicine and AAFP Guidelines on Hospice Care. We can help and do a lot; we just have to know when to stop.

References


**Figure 1: Differential diagnoses for weight loss in cats**

Recommended diagnostics will vary and may include: hematology (CBC with manual differential), serum biochemistry panel, complete urinalysis, retroviral serology, serum thyroxine measurement, serum cobalamin and folate concentrations, fecal flotations, thoracic and/or abdominal radiography, abdominal ultrasound, gastrointestinal biopsy. (modified from Laflamme DP. Nutrition for aging cats and dogs and the importance of body condition. Vet Clin North Am Small Anim Pract 35 (2005): 772.)
Figure 2: Diagnostic algorithm for anorectic cats with weight loss. Seek localizing lesion (perform diagnostics in Figure 1).

Table 1: ASA physical status classification system
The ASA classification refers to the American Society of Anesthesiologists’ classification system, based on the physical status of the patient. Five categories are defined as follows:

- Class 1: Normal, healthy patient
- Class 2: A patient with a mild systemic disease
- Class 3: A patient with severe systemic disease
- Class 4: A patient with a severe systemic disease that is a constant threat to life
- Class 5: A moribund patient not expected to survive without the operation
NASAL PLANUM DISORDERS OF THE CAT

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The most notorious disease of the nasal planum in cats is squamous cell carcinoma, however there are numerous other non-neoplastic conditions to consider when presented with a cat with an ulcerated, erythematous and crusty, swollen or even proliferative/nodular nose in this species. Because a wide variety of diseases may present with similar clinical signs, the most helpful diagnostic test (after a thorough history and physical examination) is a skin biopsy.

Neoplasia

Squamous cell carcinoma (SCC) is believed to be caused by ultraviolet (UV) light damage as light coloured (un-pigmented or lightly pigmented) cats, especially those living at high altitude, are overrepresented. Tumours occur on the nose, eyelids and ears initially looking like a smudge of dirt, a crust (actinic keratosis) progressing to a non-healing ulcer with adjacent reactive proliferation. Numerous treatments are available: surgical resection or cryotherapy are traditional mainstays of treatment, however plesiotherapy, photodynamic therapy, intra-lesional chemotherapy and combinations of these are also being used. Some recent novel treatments include:

- photodynamic therapy (PDT) using topical 5-aminolaevulinic acid showed an excellent response of 85% to a single treatment, however 2/3 of the cats had recurrence;
- PDT using the photosensitizing agent 5-aminolaevulinic acid (5-ALA) topically and a high-intensity red light source resulted in a 96% response rate but 51% of treated cats had recurrence. Those cats received a second treatment, resulting in 45% being disease free at median follow-up of 1,146 days;
- hematoporphyrin-based PDT failed to treat serious disease;
- using an accelerated proton beam radiation protocol, Fidel achieved a 60% complete response, 33% partial response and median survival of 946 days;
- superficial radiotherapy given concurrently with intralesional carboplatin resulted in complete responses in 100% of cats;
- 86% of plesiotherapy (90-Sr-Strontium) treated cats achieved complete response with one or two treatments and no recurrence of disease was seen during the follow-up period;
- in a larger group of 90-Sr-treated cats, 88% achieved complete response and a median survival of 3,076 days. As overall survival time was significantly longer for cats with a complete response to treatment than for those with a partial response, initial response to treatment appears to be predictive of overall survival time;
- a pilot study using boron neutron capture therapy was found to be safe and effective;
- a liposomal photosensitizer has been used for phototherapy of feline SCC achieving complete response rate of 100% with a recurrence rate of 20%. 
an electrochemotherapy protocol was assessed combining local administration of bleomycin (plus hyaluronidase for a more uniform distribution) with permeabilizing biphasic electric pulse. Complete response in 7 of nine cats for up to 3 years; actinic dysplasia and superficial squamous cell carcinoma involving less than 50% of the nasal planum were treated with a three-cycle curettage and diathermy resulting in complete response in 100% of cats. The probability of remaining disease free after 12 months was 0.94.

Other reports of neoplastic nasal planum disease include one in which SCC was present along with two papillomaviruses. This is interesting because in humans, papillomaviruses promote the development of SCC on sun-exposed skin. In a retrospective study of tumors of the nose and paranasal sinuses in 32 cats, there were 16 that affected the nasal planum: 15 were SCC with one being a fibrosarcoma. The SCC were treated with radiation therapy alone (11/13) or radiation following surgery (2/13). Radiation was either orthovoltage x-ray or cobalt-60. All responded completely but the tumour recurred in 11/13 with a median survival time of 12 months. The fibrosarcoma of the nasal planum was removed via cryosurgery with no recurrence 120 months following the procedure.

In a retrospective study of feline cutaneous hemangiosarcoma, one case had small raised red nodules on the nasal planum as the only site.

Immune-mediated

Pemphigus foliaceus causes pustules and crusted lesions, on the pinnae, nasal planum, periocular area, chin, and feet of affected cats. The diagnosis is made with finding subcorneal pustules with nondegenerate neutrophils and acantholytic cells on histopathology. Treatment is with immunosuppressive doses of corticosteroids alone or in combination with other immunosuppressive agents, (e.g., chlorambucil or cyclosporin). Treatment is generally lifelong.

Bergvall reported a novel ulcerative nasal dermatitis of young Bengal cats in Sweden. Lesions are limited to the nasal planum and appear as fissures, crusts, erosions and ulcers. After unsuccessful treatment with antimicrobials and corticosteroids, tacrolimus ointment resulted in improvement.

Allergic

Since the early 1990s, mosquito-bite hypersensitivity has been recognized as a cause of nasal planum disease. Clinical and histologic features suggest the diagnosis; treatment consists of indoor confinement to eliminate exposure to mosquitos (long-term) and systemic corticosteroids (short-term). Similarly, flea-bite hypersensitivity may cause crusting and pruritis of the nasal planum. Elimination and prevention of fleas along with corticosteroid therapy is indicated.
Infectious Herpesvirus dermatitis may be manifested as a progressive dermatosis on the muzzle including the nasal planum. One study attempted to treat it using recombinant interferon omega (rFeIFN-ω) perilesionally, intradermally and subcutaneously. Lesions regressed in size but did not resolve. Herpesvirus may also cause dermatitis that does not involve the face. Herpesvirus is confirmed through FHV-1 immunohistochemistry. FHV-1 PCR appears to be more diagnostically reliable for herpetic dermatitis than it does for conjunctival or corneal disease. Treatment seems to be responsive to systemic famciclovir therapy (90 mg/kg PO q8h).

Mycobacteria may cause ulceration, however they are more likely to involve the inguinal area.

Fungal organisms that may affect this part of the face include Cryptococcus neoformans and dermatophytes; extension from naso-orbital and sinuses may occur with Aspergillus sp., Penicillium sp. or Fusarium sp.. Appropriate therapy depends, to some degree, on the patient as well as the organism; itraconazole may be appropriate for cryptococcosis and dermatophytosis.

Mites, (notoedric, demodectic, otodectic, or trombicular) may be implicated.

References


While there are many similarities in ophthalmology between species, there are also species specific concerns and that is especially true in feline ophthalmology.

**Eyelids/Conjunctiva**

The most common feline eyelid abnormalities are entropion, neoplasia and agenesis. Entropion is more common in brachycephalic cats and can have a spastic component. Treatment is similar to the canine and should include both a modified-celsius and a lateral canthoplasty procedure. In addition, a lateral canthoplasty should be performed on the contralateral, unaffected eye as this has been shown to decrease the prevalence of entropion in the unaffected eye from 20% to zero.

Neoplasia of the feline eyelid is less common, but typically more aggressive than in the canine and includes squamous cell carcinoma, mast cell and fibrosarcoma as the most common tumors seen. Treatment generally includes surgical excision, but adjunctive therapy may be required. Interesting, it is noted that even with incomplete excision, the prognosis for mast cell tumors of the feline eyelid remains excellent.

Eyelid agenesis is a congenital abnormality typically affecting the superior-temporal eyelid margin. A complete ophthalmic examination is indicated as other congenital ocular abnormalities may be concurrent and include dermoid, persistent pupillary membranes, cataract, coloboma and others. Treatment of eyelid agenesis is indicated if corneal health is compromised. While numerous surgical options have been described, the lip to eyelid transposition works best as it provides skin, muscle, mucosa, a mucocutaneous junction and ensures the direction of hair growth of correct.

Feline conjunctivitis is common and typically infectious in origin. Common differentials include chlamydia, Herpes, mycoplasma and bartonella. History, physical examination, fluorescein staining and cytology are all indicated. In chronic non-responsive conjunctivitis, bartonella should be considered.

**Cornea**

The most common feline corneal abnormalities include ulcerative keratitis, corneal sequestration and eosinophilic keratitis. Ulcerative keratitis is most often herpetic in origin and may have secondary bacterial opportunists. Treatment should include stress minimization, oral or systemic antivirals (fameclovir, cidofivir), oral L-lysine and some will also use interferon and probiotics in addition to standard therapy.
Corneal sequestration is seen in association with herpes keratitis, secondary to chronic ulceration and can be iatrogenic when topical corticosteroids are used in cases of active herpes keratitis or when a grid keratotomy is performed. Both of the latter are contraindicated in cats. Treatment for corneal sequestration, if painful, is a superficial keratectomy with or without adjunctive grafting procedures.

Eosinophilic keratitis is a non-ulcerative, proliferative keratitis. Treatment may include topical cyclosporine, topical corticosteroids or oral megesterol acetate.

**Uvea**

Common diseases of the anterior uvea include uveitis, glaucoma and neoplasia. Uveitis can be ocular or systemic in origin. Ocular causes include ulcerative keratitis, lens-induced, ocular trauma and primary intraocular neoplasia. Systemic etiologies for feline uveitis include infectious (FeLV, FIV, FIP, mycotic, toxoplasmosis, bartonella, other), secondary neoplasia and immune/idiopathic etiologies. It is important to note that the infectious etiologies are not mutually exclusive and infection with more than one disease is not uncommon.

Feline glaucoma is most often secondary to chronic uveitis. Breed-associated glaucoma may be noted in the Siamese, Burmese and European shorthair, but is uncommon. Glaucoma secondary to uveal cysts is also seen and is best managed using transcorneal diode laser to ablate the cysts.

Uveal neoplasia can be primary or secondary with secondary as result of lymphosarcoma most common. Primary uveal neoplasia includes melanoma, adenoma, adenocarcinoma and spindle cell sarcoma. While there is suggestion of malignancy for anterior uveal melanoma, these more commonly are locally problematic and enucleation is often curative and is advised when the mass is raised, progressive and/or associated with secondary intraocular disease. Malignant spindle cell sarcoma arises from the lens epithelial cells following chronic uveitis, cataract or intraocular trauma. It is highly aggressive, malignant and often fatal. Enucleation should be considered for feline eyes that are blind secondary to chronic trauma or uveitis.

**Posterior Segment**

Inflammation of the posterior segment, termed chorioretinitis, has the same systemic differentials as anterior uveitis. In addition, non-inflammatory abnormalities of the retina include detachment and degeneration. The most common etiology for feline retinal detachment is systemic hypertension. Retinal degeneration can be primary as seen with Progressive Retinal Atrophy or secondary to inflammation, nutritional deficiency, glaucoma or iatrogenic secondary to systemic enrofloxacin.

**References**


SNOTS & SNUFFLES:
THE CAT WITH CHRONIC UPPER RESPIRATORY DISEASE

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It is a frustrating to treat the chronic snuffer. A logical diagnostic plan to differentiate probable etiologies and to rule-out non-viral causes results in appropriate therapeutic choices. Even with a viral etiology, non-specific therapies to reduce the pathological consequences of infection may modulate clinical signs.

HISTORY & PRESENTATION - Chronic, recurrent rhinosinusitis occurs in cats of any age. Knowing the timing, onset, duration and frequency of sneezing can be helpful. With chronicity, sneezing may be abolished resulting in accumulation of discharge. Nasal discharge may be serous, mucoid, purulent, or sanguinous. It is helpful to know whether the discharge has changed, whether it changes throughout the day or season, and whether it is unilateral/bilateral. Some cats have seasonal flare-ups suggesting an allergic or contact irritant component.

Respiratory patterns and sounds may be abnormal. Clients may comment on the cat sounding hoarse, silent when meowing or that the purr has changed. In general, sounds heard on inspiration come from larger airways whereas expiratory sounds are from smaller, lower airways. Snorting reflects accumulation of discharges in the nasal passages or with secretions coughed into the oropharynx. Snoring/stertor are associated with proximal upper respiratory occlusion, (e.g., polyp, foreign body obstruction or functional inflammatory obstruction). Stridor is an inspiratory wheeze reflecting changes in the larynx. An expiratory wheeze, crackles and rales caused by small airway involvement. A lack of bronchovesicular sounds occurs with pulmonary consolidation or inflammation.

Assess facial symmetry (face-on and from above). Palpate the face to look for swelling, invagination or discomfort. Look at teeth and alveolar bone for periodontal disease, abscessation or inflammation, ulcers, masses and polyps. Evaluate nasal passage patency using a small mirror, a glass slide or wisps of cotton. Auscult and palpate the trachea to see if a cough is elicited. Auscultation of the frontal sinus with a pediatric bells may be revealing. For pulmonary auscultation, use two heads, the standard bell and a plexiglass scope as they have different sensitivities and frequencies.

Fundic examination should be performed to look for Cryptococcus and other signs of systemic disease. Enlargement of regional lymph nodes or generalized node enlargement should be assessed.

ETIOLOGY AND PATHOGENESIS - Chronic rhinitis may be a sequel to, or separate from, acute rhinitis. It may represent an ineffective immune response to persistent viral infection. Feline herpesvirus 1 (FHV-1) may be the common denominator initiating turbinate resorption, with subsequent secondary bacterial infections and unchecked inflammation.
exacerbating the problem. This is especially bad in anatomically-predisposed individuals (conformation, anomalies). Irreversible destruction of the turbinates may result in viral or inflammatory mediator-induced cytolysis. Reactivation of herpesvirus from infected trigeminal ganglion may result in recurrent destruction.

Other viruses (e.g., calicivirus) and bacteria (e.g., Bordetella bronchiseptica, Chlamydophila felis, Mycoplasma spp. anaerobic organisms) may be implicated. The fact that cats on antibiotics often improve clinically supports the role of bacteria, however, when signs recur, despite therapy, bacteria are only part of the cause of the illness. When antimicrobial therapy of 7-10 days fails to result in resolution, a thorough diagnostic work-up is warranted.

The main fungal organisms causing chronic upper respiratory disease (URD) are Cryptococcus neoformans var. neoformans and gattii (>Aspergillosis sp., Penicillium spp). These cause severe inflammation, facial deformity and skin ulceration along with unilateral (> bilateral) nasal discharge. Trauma, congenital and conformational aspects, polyps, periodontal disease and foreign bodies all predispose to chronic infection as may neoplasia.

**DIAGNOSTICS** - A minimum database consists of a CBC, serum biochemistry, retroviral serology, urinalysis and blood pressure determination. If rhinoscopy is considered or if epistaxis has been part of the process, a coagulation panel should be performed and any medications affecting hemostasis should be temporarily discontinued.

Skull radiography or CT/MRI to image dentition, nasal passages and sinuses as well as bone health requires general anaesthesia. Probe all periodontal pockets, retract the soft palate to look for polyps and palpate the soft palate. Three standard radiographic views should be exposed using high detail films and screens. Following imaging, samples should be harvested. Unfortunately, cytology does not appear to be a reliable means for the detection of chronic inflammation and evaluation of chronic rhinitis in cats.

During rhinoscopy, irrigation with sterile saline is essential. Mucus exudation, a polyp or mass, foreign body or “webbing” (nasopharyngeal stenosis) may be seen. If unilateral disease is present, evaluation of the unaffected side first is recommended. Normal turbinate mucosa should be pale pink and smooth. Hyperemia, irregular turbinate surfaces and moderate amounts of discharge suggest pathology. Even if the mucosa looks normal, biopsies should be taken in a cat with chronic disease, as gross appearance may be misleading.

Aerobic and anaerobic cultures may be set up but results must be interpreted with caution because there are large numbers of normal flora in the nasal cavity. One can improve diagnostic yield by obtaining cultures from deep within the nasal cavity avoiding superficial contamination.

**THERAPEUTICS: SPECIFIC** - Practitioners frequently choose antibiotics empirically to treat the cat with URD. However, interpretation of an aerobic culture may not be simple: the significance of the growth is questionable when multiple organisms are grown but if a single species is grown that is NOT a normal commensal, sensitivity results may be used. Therapy should be continued for 6-8 weeks without changing the antibiotic if there is an initial
positive response; the antibiotic should be safe for long-term use and must penetrate mucus and cartilage. Doxycycline is generally effective against Chlamydophila and L-forms. Azithromycin (5-10 mg/kg PO q24h for 5 days, then q72h long term) has a long duration of action however may not be effective. Administration of antibiotic ophthalmic drops can be used as direct topical therapy to the nasal passage. Ophthalmic administration of alpha interferon in saline has been recommended for cats with herpes virus keratitis or conjunctivitis. Acyclovir is an anti-herpes drug potentially toxic in cats: famcyclovir is preferable: 15mg/kg PO q12h (62.5 mg) (up to 90 mg/kg PO q8h) X 2 weeks, assess response and decide whether or not to continue.

**THERAPEUTICS: NON-SPECIFIC** - Maintaining hydration is essential for tissue perfusion, to make secretions less viscous and to improve cell function. Humidifying the air around patients is beneficial. Oral and nasal decongestants doses are listed (Table 1). Nasal flushing is helpful. With a cuffed endotracheal tube in place, large volumes (100-300 cc) of warmed, sterile saline are infused into one nostril while occluding the other. Adequate nutrition (quality, balance and quantity) is critical. Appetite stimulants may help short-term: (cyproheptadine: 1 mg PO q12h); mirtazapine: 2-4 mg/cat PO q72h).

Anti-inflammatories play a role. By reducing airway swelling, breathing improves and less secretion is produced making the patient more comfortable. The concern with the use of glucocorticoids is the possibility that they might result in recrudescence of the virus or virus shedding. Non-steroidal anti-inflammatories are alternate options; they should be given with food and dosed based on lean body weight. Piroxicam (0.3 mg/kg PO q48h) or meloxicam (0.05 mg/kg q24h) may help. Leukotriene blockers may also be considered to reduce inflammatory cell infiltration.

**PROGNOSIS** - It is important that clients understand that a cat with chronic rhinitis will never be cured. With on-going management, quality of life can be improved with a reduction in sneezing and nasal discharge.

**Table 1: Feline Upper Respiratory drugs and doses**

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<tr>
<th>Antihistamines</th>
<th>SID X 3 days only to avoid rebound congestion)</th>
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<tr>
<td>Amitriptyline: 5-10 mg/cat q12-24h</td>
<td>(Oxymetazoline or 0.05% xylometazoline)</td>
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<td>Chlorpheniramine: 1-2 mg/cat q12-24h</td>
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<td>Clemastine: 0.05 mg/kg q12h</td>
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<td>Cyproheptadine: 1 mg/cat q12h</td>
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<td>Diphenhydramine: 2-4 mg/cat q8-12h</td>
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<td>Hydroxyzine: 2.2 mg/kg q8-12h</td>
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<td>Trimethazine: 0.5-1 mg/kg q8-12h</td>
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<td>Cetirizine: 5 mg/cat q12h</td>
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<td>Fexofenadine: 10 mg/cat q12h</td>
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<td>Claritin: 0.5 mg/kg/day</td>
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<th>Decongestants:</th>
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<td>Dimenhydrinate: 4mg/cat PO q8h</td>
</tr>
<tr>
<td>Pseudoephedrine: 1 mg/kg PO q8h</td>
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<tr>
<td>Nasal decongestant drops: 1 drop per nostril</td>
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HAIRBALLS: JUST A HAIRY NUISANCE OR A SIGN OF DISEASE?

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Hairballs typically present as a tubular wad of tightly or loosely packed ingested hair. Clients may use the term hairballs to describe loose strands of hair in vomitus containing clear or coloured liquid or strands of hair within regurgitated or vomited food. They may report that their cat extends his/her neck and appears to cough before dispelling the hairball +/- liquid. This behavior may, in fact, be a sign associated with small airway disease/“asthma”. It is therefore important to determine exactly what the client is witnessing before determining what diagnostic and therapeutic approach to take. In the extreme situation, a true trichobezoar, which is a hard concretion consisting of hair, lodged in the esophagus of stomach, is too large to vomit or to pass through the pylorus and intestines.

Cats routinely ingest small amounts of hair through grooming; this normally passes in the feces. When this process is disrupted either due to increased ingestion or abnormal passage of hair (i.e., changes in gastrointestinal motility), hairballs ensure. It is therefore important to try to identify and treat the underlying cause of the hairball rather than just its resulting effect. Psychogenic or behavioural causes should also be considered.

Empirical treatment

While there are numerous therapeutic recommendations and commercial diets to reduce the frequency of vomiting hairballs, the underlying cause should always be addressed.

Hydration

- Optimizing hydration by utilizing moist food, adding water to meals, and administering subcutaneous fluids will help to normal cellular and neuromuscular function thereby improving gastrointestinal (GI) motility.

Hairball remedies

- These consist of malt-flavoured petroleum with or without added vitamins. These products can be used copiously (1/3 tube) in the short term and daily or intermittently at maintenance doses (2-5 cm/day) long term.
- Treats and diets containing beet pulp and other fibers may help to normalize intestinal motility.

Remove excessive loose hair to prevent hairball formation

- Combing and brushing may help, however there is often a superficial layer of loose hair left behind that the cat will swallow when completing the job. Wiping with a damp paper towel helps to remove these fine fibers. Comb/brushes such as the Furminator® will reduce the quantity of hair but must be used cautiously to avoid removing too much fur.
Ensure that medications do not get stuck in the esophagus

- Drugs such as oral clindamycin and doxycycline pills/capsules can cause irritation and may result in oesophageal strictures. It is prudent to flush any oral medication not in a liquid formulation with a 3-6 ml water chaser.

Diagnosis and treatment of underlying cause

Oesophageal diseases

- Radiographs should be taken. Displaced viscera may be seen suggesting a congenital problem or previous trauma; megaesophagus may be seen. A contrast imaging study (barium meal) can be used to identify oesophagitis (abnormal striations), a stricture or a foreign body, such as a hairball within the oesophagus or stomach.
- Endoscopic evaluation may be indicated to look for a stricture, to biopsy a mass or to remove a foreign body. Fluoroscopy may be required to study a dynamic process such as a sliding hiatal hernia.
- Treatment will depend on the condition discovered. Correction or alleviation of the underlying problem will result in a reduction or cure of the hairball problem.
- Medical therapy for oesophagitis includes reduction of exposure to acid using an H2 antagonist (e.g., famotidine: 5 mg PO q24h) or proton pump inhibitor (e.g., omeprazole: 1.0 mg/kg PO q24h). Sulcralfate (0.25g PO q8-12h) may help coat the denuded mucosa and must be given 20-30 minutes before reducing acid levels. Analgesia should be considered; gastrostomy tube feeding may be necessary in severe cases.
- Oesophageal strictures may require balloon dilation to break down fibrosis.
- Medications should be in liquid format if given orally to avoid causing or exacerbating oesophagitis.

Gastric and intestinal diseases

- Radiography, ultrasound and endoscopy may be performed non-invasively. Ultrasound has the advantage of assessing motility.
- Gastric foreign bodies (including trichobezoars) will require surgical removal.
- Biopsies may be required (laparotomy or endoscopy) to determine the cause of reduced motility or ileus.
- Fecal examination or routine use of a broad-spectrum anthelminthic is recommended.

Pancreatic disease

- Ultrasound in combination with serum fPLI is the least invasive way to diagnose pancreatitis.
- General treatment of pancreatitis consists of providing analgesia, fluid therapy and ensuring that the patient receives adequate amounts of balanced diet.
Biliary tree disease

- Radiography may reveal an opacity in the region of the gall bladder. Ultrasound of the biliary tree will confirm the presence of choleliths and will also reveal any sludge and/or cholecystitis.
- Aspiration of bile for cytology and culture may be performed under ultrasound guidance. Bile cytology may show infection and/or inflammation. Antibiotics should be chosen according to the results of sensitivity testing, however when finances are a limiting factor, use of metronidazole for anaerobic bacteria along with a fluoroquinolone for gram positive and negative aerobes should be considered.

Lower urinary tract disease

- Urinalysis will be helpful by revealing whether or not infection, inflammation, idiopathic disease or crystals are present.

Dermatologic diseases

- Over-grooming may be generalized rather than restricted to one region when skin is the affected organ. When ectoparasites, mites, and dermatophytes are not seen, after flea treatment has been performed, skin biopsies (to detect allergy) may be warranted.

Degenerative joint disease and spondylosis deformans

- Asking appropriate questions regarding mobility, jumping and climbing (both up and down) as well as overall energy may suggest the presence of degenerative skeletal diseases (DSD). Radiographs may be taken to identify affected joints although radiographic findings do not always correlate with clinical findings and normal radiographs cannot rule out the presence of DSD. Disease modifying agents such as glucosamine/chondroitin sulfate and therapeutic diets in conjunction with appropriately used NSAIDs and other analgesic agents is indicated.

Psychogenic distress and behavioural considerations

- Cats may express over-grooming as a way to self-soothe when stressed. This stress may be social (associated with other individuals [human, cat, dog, etc.] in the home), frustration (a change in or loss of routines) or environmental (inadequate opportunities to express normal cat-appropriate behaviours). Individuals with compulsive/obsessive temperaments will start to over-groom and then be unable to stop the behaviour once it is initiated. They may restrict excessive grooming to just one region (e.g., the fore limbs or ventral abdomen) or may generalize the behaviour.
- Evaluate the household structure and routine as well as the presence and placement of resources (perches, hiding places, feeding stations, water stations and latrines).
- Antianxiety therapy (pheromones, diet, drugs) may be recommended.
FELINE EOSINOPHILIC GRANULOMAS: COMPLEX OR MAYBE NOT?

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The eosinophilic granuloma complex (EGC) has a history of being confusing to veterinary dermatologists and practitioners alike. Since 1975, based on clinical and histopathologic criteria it has been divided into three separate entities: the indolent (or eosinophilic) ulcer, the eosinophilic plaque and the eosinophilic granuloma. While a large number of etiologies have been attributed to these lesions, the majority appear to be allergic in nature. Response to treatment has, in some cases, been frustrating with non-responsive or relapsing lesion, while in others, lesions have resolved spontaneously1.

Clinical features: characteristically, lesions are firm, well-circumscribed papules (intradermal) or nodules (extending beyond the dermis into the subcutis). Initially, the overlying skin and hair coat appear normal, however, over time alopecia develops and the lesions become discoloured (erythematous, yellow, orange). These often ulcerate and have a serous crust1. Three presentations are recognized:

1. When located at the mucocutaneous junction of the upper lip, either uni- or bilaterally, initially a shallow ulcer, these lesions are known as “indolent-”/”rodent-”/”eosinophilic-ulcers”. They are raised, well demarcated, occasionally eroding the upper lip dramatically. They do not appear to be pruritic.
   a. Differentials include focal trauma or neoplasia (squamous cell carcinoma [SCC], mast cell tumour)2.

2. “Eosinophilic plaques” may be found in any haired location, most commonly on the ventral abdomen, face, neck, inguinal region, thighs (medial and caudal) or on the pads of the paws. They are well demarcated, erythematous, raised, often alopecic, flat-topped plaques. They may be covered with a serous crust and are intensely pruritic. In some cases they look like coalescing military dermatitis lesions3.
   a. Differentials include dermatophytosis, neoplasia (lymphoma, mast cell tumour, SCC, mammary adenocarcinoma), cutaneous viral disease (FHV-1), mycobacterial or fungal infection2.

3. The granulomatous variant may present as a well demarcated, raised, hard, non-inflammed, erythematous linear lesion (“linear granuloma”) on the caudal thigh. They may also appear as firm nodules in the interdigital spaces or on foot pads. Alopecia may be present. If affecting the chin, a range of presentations is seen from a soft swelling (“fat”/”pouty” lower lip/chin) to a hard, even ulcerated lesion exuding yellow-white gritty material. Small popular lesions occur uncommonly on the pinnae. Unless ulcerated, the
cat doesn’t appear to be perturbed by this form. Oral lesions may be raised or ulcerated on the tongue or palate; in the latter case, significant, (but inapparent, as swallowed) blood loss may occur if ulceration involves blood vessels of the hard palate.

a. Differentials include all of those listed for eosinophilic plaques as well as bacterial folliculitis/furunculosis or abscess, foreign body reaction or sterile granuloma².

Distribution: In one study of 55 cases of idiopathic eosinophilic granuloma, 42% of the cats had lesions were found on lips (+/- commissure or chin with one having lesions on caudal thighs and one with fore paw pad lesion). Twenty-two percent of cats had caudal thigh lesions, 18% had chin lesions. Eight-two % of cats had lesions in more than one location¹. The incidence of EGC among 1407 feline patients seen by this dermatology service, for which follow-up was available, was 4%⁴.

**Etiology:** In the majority of cases, EGC is a hypersensitivity (hs) reaction to environmental allergens, (atopic dermatitis), food, insects (fleas or possibly mosquitoes, although mosquito-bite hs is probably a separate disease entity). Feline self-allergens have also been suggested as a cause (antibodies to epithelial components⁵ or Fel d 1 (a salivary allergen)⁶: if Fel d 1 is involved, it is likely that exposure is through grooming already abnormal skin.

Other, less common causes include mites, bacteria (e.g., Staphylococcus), dermatophytes, feline herpesvirus-1 (FHV-1), and foreign bodies (plant or insect parts, hair shafts). It is difficult to know whether intracellular bacteria seen on cytology are causing the reaction or whether the tissue has become infected secondary to the tissue damage. Two studies suggest a genetic predisposition (eosinophil dysregulation) in some cats when exposed to allergic triggers⁷-⁹.

**Diagnostics:** Despite the majority of lesions of the EGC having an allergic component, it is important to confirm the diagnosis in order to rule out the differentials that might not respond to or be made worse by immunomodulatory therapy². Cytologic samples may be harvested by making touch impressions of ulcerated lesions with glass microscope slides. When large numbers of eosinophils are found, EGC is strongly suggested. When intracellular bacteria are seen in neutrophils, culture and sensitivity is recommended. Other tests include Wood’s lamp examination (performing fungal culture on appropriate hairs) and microscopic examination of skin scrapings. Surgical biopsies are warranted in non-ulcerated lesions as well as some ulcers, especially those in the oral cavity.

The presence of concurrent systemic disease may affect therapeutic choices. A minimum database of a complete blood count (CBC), serum biochemistries, FeLV and FIV serology and urinalysis should be included in the work-up. A peripheral eosinophilia occurs in some, but not all cats. If high doses of cyclosporin are being considered, a toxoplasmosis titre is indicated: cats with pre-existing titres are unlikely to manifest recurrence of latent disease whereas those who do not have antibodies may be a risk for developing disease if exposed during treatment with this agent².
Unless evidence of fleas is noted, an ectoparasite elimination trial should be performed over 6-8 weeks. All in-contact animals should be treated as well for the same time period. Environmental contamination must be considered as a source of reinfection.

A strict dietary trial using a novel protein or hydrolyzed protein diet should be instituted restricting the patient to this diet for a full 6-8 weeks.

While controversial, serum allergy testing or (if appropriate), intradermal skin testing may be considered. This can be helpful in order to determine which allergens should be avoided in the atopic individual.

**Therapy:** Unless primary disease is identified for which specific treatment exists (e.g., itraconazole for dermatophytosis, avoidance of trigger dietary allergens or fleas), immunomodulatory therapies for feline allergic disease are indicated. These include glucocorticoids, cyclosporin, chlorambucil and essential fatty acids.

Oral prednisolone is preferable to injectable daily dexamethasone or methylprednisolone acetate as the dose can be titrated to effect and the risk of complications, including that of developing diabetes mellitus, is lower. Initial dose is 1-2 mg/kg PO q24h; some patients may need higher doses. Once lesions have resolved, the dose should be tapered to the lowest effective alternate day dose.

Cyclosporin at 5 mg/kg PO q24h is as effective as prednisolone at 1 mg/kg; higher doses may be needed. After a four-week course of therapy, treatment is tapered to alternate day with eventual twice-weekly treatment. Numerous drug interactions are known, therefore when other agents are indicated that might compete for cytochrome P 3A enzymes, the dose should be reduced.

Chlorambucil can be given concurrently with prednisolone at 2 mg/cat PO two-three times a week. It may also be considered as a sole agent when lesions are refractory to corticosteroid therapy or in a patient in which corticosteroids are contraindicated. Because of the possibility of reversible marrow toxicity, CBC should be monitored every two weeks for the first three months of use.

Omega 3:6 fatty acids may prove beneficial as adjunctive therapy by dampening inflammatory cascade as well as improving skin barrier function.

One author has suggested, based on follow-up of 55 cases of idiopathic EGC, as only 22% received treatment yet all cats went into remission over a period of one to nine months, that spontaneous resolution of lesions may occur. When underlying etiology is allergic and the offending allergen cannot be eliminated, immunomodulation is, however warranted.

**References**


PARASITIC SKIN DISEASES – CLINICAL CASES PRESENTATION

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Skin diseases caused by parasites play very important role in canine and feline dermatology. Approximately every third or fourth dermatological problem in small animals is caused by skin parasites. Although in many cases is proving of parasite relatively easy, it could be a challenge from the point of differential diagnosis of many different conditions. Despite of the broad spectrum of antiparasitic agents there are relatively high number of patients were “classical” therapeutic protocols fail – usually as a result of underestimating some critical factors. On the top of it there is necessary to realize that some of dog’s and cat’s skin parasites have certain zoonotic potential. Case presentation is focused on canine demodicosis, sarcoptic mange, cheyletiellosis and cat’s and dog’s ear mite infestation.

Canine demodicosis is in our conditions the third most common parasitic skin disease. The most important role plays Demodex canis, less frequently is found Demodex injai and Demodex cornei which lives in superficial epidermal layers. Inherited immunodeficiency and/or immune-compromised conditions (excessive glucocorticoid therapy, hyperadrenocorticism, neoplasia, diabetes mellitus etc.) play crucial role in excessive multiplication as well as clinical manifestation of disease. In the differential diagnosis of dog’s folliculitis we consider demodicosis as one of the most important. Therapeutic approach should respect many criteria and should be tailored to each individual. Demodicosis represents no risk for humans.

Sarcoptic mange is highly contagious disease caused by the mite Sarcoptes scabiei varietas canis (S. canis) and in scale of skin parasitic diseases of our dog’s patients it occupies the fourth position. The life cycle lasts for about two weeks and despite of the fact it is one of the most pruritic diseases it is frequently underdiagnosed. There is necessary dozens deep skin scrapings to prove either mite eggs, or feces. The most specific skin changes are usually at the ear margin, elbow & hock area. Changes at the ventral aspect of the body are typical for young animals. There are two problems regarding of sarcoptic mange: (1) Because is often overlooked is treated as some unknown hypersensitivity, (2) Sarcoptes scabiei var. canis has reasonable zoonotic potential. Therapy is so far usually successful reinfection relatively common.
Cheyletiellosis is a highly contagious disease caused by fairly species-specific mites of a dog (Cheyletiella yasguri) and a cat (Cheyletiella blakei). In descending order, it occupies the fifth position among parasitic skin diseases of our patients. It is quite frequent, especially in puppies and kittens coming from kennels, pet shops, or living in non-optimal hygienic conditions. The life cycle takes about three weeks. Cheyletiellosis is also a pruritic skin condition, and despite the declared dandruff surplus and the use of different diagnostic techniques (Scotch tape, coat brushing, superficial skin scraping, etc.), proving of parasites or their eggs attached to hairs could be a challenge. Formerly presented easy therapy and preventive measures are not always truthful in many cases. Cheyletiellosis is considered as a zoonosis and temporarily affects as many as 50% of humans living in close contact with an affected animal.

Ear mite infestation (Otodectosis) is caused by Otodectes cynotis which is also highly contagious mite living predominantly in the ear canals. Otodectes is definitely number one in the etiology of otitis in a cat and plays also an important role in a dog where it is commonly underdiagnosed. Therapy and preventive measures frequently fail in large-scale breeds and in breeds where outdoor cats are present.

Above mentioned parasitic conditions are presented at clinical cases.

References are available upon request.
Hypothyroidism, namely its primary form is probably commonly overdiagnosed diseases. It is because great difficulty in accurate diagnosis, presence of so cold euthyroid sick syndrome, simultaneous therapy and other factors. Acquired hypothyroidism usually occurs in the adult animals secondary to autoimmune lymphoplasmacytic thyroiditis. It is a complex metabolic disorder resulting from inadequate thyroid hormones production. Thyroid hormones affects wide range effect on cellular metabolic activity and any alteration influences many organ systems, so hypothyroidism is without any doubts systemic diseases.

Clinical manifestation is usually slow and discreet and many dog’s owner assume it as a result of ageing. General status, dermatological symptoms and neurological changes are demonstrably resulting from the impaired thyroid function. Affection of other organ systems (cardiovascular, reproductive malfunctions etc.) or clinical symptoms (megaoesophagus, uveitis, irritability, aggression, obesity etc.) are often derived from clinical symptomatology of human’s hypothyroidism and direct impact thyroid insufficiency isn’t completely elucidated. Classical dermatological symptoms connected with dog’s hypothyroidism are slowly developing non-pruritic symmetrical alopecia affecting trunk, neck and other friction areas. One of the first skin symptoms is progressive alopecia on the dorsum nasi which is later joined by tail alopecia (so cold rat tail). Alopecic skin becomes hyperpigmented or depigmented. Remain hairs are thin easily epilated and almost all are in telogen developmental stage. Hairs regrowing if any are very slow. Recurrent chronic pyoderma is often observed in dog’s hypothyroidism probably as a result of impaired cutaneous defense.

Neuromuscular signs of a dog’s hypothyroidism comprise polyneuropathy, peripheral vestibular syndrome, slow reflexes, muscle weakness, paresis n. facialis, Horner’s syndrome and some other neuromuscular symptoms.

Functional hypothyroidism (euthyroid sick syndrome) results from an interaction between variety of diseases and drugs and thyroid functioning. There is known thyroid hormone level is inversely proportional to age and dog’s body weight. In some breeds (e.g. Greyhound, Deerhound) are physiological thyroxine levels much lower than in majority dog’s population. Main conditions influencing level of thyroid hormones are e.g. chronic infection, Cushing’s disease, diabetic ketoacidosis, hepatic & renal insufficiency, (neoplastic) cachexia, Addison’s disease and others. Many drugs (glucocorticoids, phenobarbital, furosemide, clomipramine diazepam etc.) also reduce basal T4 and/or T3 levels.
Routine hematology can show non-regenerative, normochromic, normocytic anemia and in biochemistry panel could be increased cholesterol.

There are available many hormonal assays which can be used in diagnosis of hypothyroidism but from practical point of view we recommend following advices:

1. Measuring total T4 (tT4) level. All findings of tT4 below 10 nmol/l are for dog’s hypothyroidism highly suggestive. Total T4 levels of 10 – 20 nmol/l are not easy to interpret. We always should compare it with the level of canine thyroid-stimulating hormone (cTSH) and, of course, take in account possible functional hypothyroidism, current therapy etc. In case of doubts we recommend repeat measuring in a few months. Levels of tT4 which are well in normal values, e.g. 35 nmol/l or higher are very unlikely in patients suffering from adult hypothyroidism. Comparable results we can reportedly get by using free T4 (fT4). Our experience in this field is limited.

2. Measuring canine thyroid-stimulating hormone (cTSH) level. Interpretation should be in correlation to clinical status and T4 level. All values above 0.5 mg/ml may be consistent with dog’s hypothyroidism but do not use cTSH as a single diagnostic method. Take in account that there is necessary to use species specific, i.e. canine TSH. Human assays are not suitable.

Diagnostic obstacles are documented in four clinical patients.

References are available upon request.
CASE REPORT – CSK IN GERMAN SHEPHERD AND ITS RELATIONSHIP TO ENDOCRINOLOGY

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Presented German Shepherd, 4 years old, spayed female, NICKY, referred for bilateral ocular changes without successful treatment with antibiotic ointment. Status quo: vascularisation of temporal quadrant of the limbal conjunctiva and hypergranulation of „fibrovascular“ appearance, structural changes of the corneal stroma spreading from limbus towards the center of the cornea, pigment deposition in the superficial corneal layers, and conjunctival depigmentation of the nictitate membrane. We did clinical and ophthalmologic examination focused on assessment of eye status and eye adnexa, including Schirmer teat test (STT), corneal staining with fluorescein and biomicroscopic examination using a slit lamp. Fluorescein staining was negative, STT production 14 mm/min. For diagnose of hypothyroidism, blood concentrations of total tT4 and specific canine thyreotropin cTSH were determined.

Female was treated with one subconjunctival injection of 6 mg 1% prednisolone with 20'000 i.u. gentamicin and further local treatment with cyclosporin 2% eye drops BID and 0.5% hydrocortison ointment SID for 6 weeks.

Hypothyroid female (tT4 9.4 nmol/l within the reference limit of ≥ 20 nmol/l, cTSH 0.69 ng/ml within the reference limit of ≤ 0,5 ng/ml) was additionally subjected to a substitution therapy with L-thyroxin at an initial dose of 5 μg/kg BID for 2 weeks. The dose was subsequently increased to 20 μg/kg/day and the next visit for potential dose adjustment followed 12 weeks after start of local eye treatment. At this occasion, the ocular changes (neovascularisation, hypergranulation, hyperpigmentation and nictitating membrane changes) were also assessed.
SKIN HYPERSENSITIVITIES – PRACTICAL MANAGEMENT

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Successful management of a dog suffering from any form of hypersensitivity depends on identification of its etiology, pathogenesis severity of clinical manifestation and should be tailored specifically to each individual.

Respecting current terminology it seems to be valuable to present definition of more or less immunological terms. Hypersensitivity – reproducible clinical sings, triggered by exposure to a stimulus which, at the same dose, produces no effect in a normal individual. Allergy – hypersensitivity of immunological origin. Atopy – predisposition to develop allergic reactions. Canine atopic dermatitis – a genetically-predisposed pruritic dermatitis characterized by particular patterns of lesion distribution and frequent association with allergy to aeroallergens.

From the practical point of view we should initially take in account all skin conditions connected with pruritus which is undoubtedly the main reason for presentation at a veterinary dermatology. Pruritic dogs are mostly scratching, cats prefer licking and list of differential diagnoses of pruritus is extremely wide. History has to be extensive enough and we should consider breed, age of onset, lifestyle and environment, diet, pre-existing illness, onset of clinical signs, early lesions distribution, seasonality, evidence of transmission to other in-contact animals and/or humans, response to previous therapy etc. Clinical examination is most important and should cover general examination (e.g. symptoms associated with atopy like conjunctivitis and rhinitis; food hypersensitivity like vomiting and diarrhea), extensive dermatological examination (differentiation is beyond of this presentation) and routine diagnostic tests (skin scrapings, Scotch tape test, coat brushings, impression smears).

Using above mentioned approach we are able to identify and successfully treat almost all parasitic skin diseases including successful control of flea allergy dermatitis, foreign bodies, pyotraumatic dermatitis, Malassesia infection and many other conditions, e.g. source of musculoskeletal pain and behavioral disorders. Skin biopsy could help us to identify many skin tumors, autoimmune diseases but in cases of hypersensitivities has limited value.

Intradermal skin testing and some relevant serology are essential in order to select allergens for desensitization in the atopic dog. Rapid screening serological tests should be avoided as their positive and negative predictive values are poor.

Elimination diet represents the next step. It should be carried out and followed strictly for at least 6 to 8 weeks. A third of atopic dogs can be controlled with diet.
The aim of intradermal testing is to reproduce locally the hypersensitivity phenomenon by injecting individual allergens. Intradermal testing has only been validated for aeroallergens. Using allergenic extracts which are too complex (e.g. house dust) brings many complications for proper interpretation.

Management of hypersensitivities is because of its complexity and multifactorial conditions should follow etiology and from the general guideline (flea control, well-balanced diet, antifungal and antiseptic shampoos, emollients, moisturizers, regular grooming, ear control, antibiotic therapy, *Malassezia* control, essential fatty acids, glucocorticoids, tacrolimus, cyclosporine A, allergen avoidance, anti-allergen vaccination) should be chosen convenient parts. This approach is demonstrated at clinical patients. Longstanding and close cooperation with an owner is also essential.

**References are available upon request.**
SUNLIGHT INDUCED SKIN TUMORS

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As the skin is the largest organ in the body, it is perhaps unsurprising that skin tumors represent one third of the tumors diagnosed in dogs. The incidence rate of skin tumors has been increasing in through the past decades (1960-2000), representing 1.9% to 3.6% of tumors diagnosed in dogs examined at veterinary teaching hospitals in North America. Sunlight associated malignancies are most typically squamous cell carcinomas (SCC) account for the 1.25-15% of all cutaneous tumors in dogs. In cats, SCC accounts for the approximately for 15-50% of all cutaneous tumors and this is among the four most common feline skin tumors, along with basal cell tumors, mast cell tumors and fibrosarcomas. Common locations for SCC in dogs are nasal planum and nail bed. Indeed, SCC accounts for 33-50% of subungual tumors in dogs, where the lesions occur in dogs with black hair coats most commonly. This is as opposed to locations associated with ultraviolet sunlight exposure, such as on the flank, medial thighs, or abdomen in the skin of short-coated, lightly pigmented dogs. The most common location of SCC in cats is the head, where 57-65% may be observed on the ear pinna. Other common sites included nasal planum, eyelids, pre-auricular area, and lips. Other sunlight-induced lesions include cutaneous hemangiosarcoma in dogs and cats, and in dogs dermal melanoma, and possibly basal cell carcinoma in some individuals. These lesions have in common their location in areas of the body that are chronically sunlight-exposed, sparsely haired and not protected by pigmentation.

Cutaneous SCC (cSCC) commonly affects older dogs and cats, with a mean of 8 and 12 years of age, respectively. There appears to be no gender predilection. Overall, cSCC is most common in animals without pigmentation in areas of sparse haircoat. There is a reported 5-13 times higher incidence in white-coated than in pigmented cats. Similarly, cSSC are overrepresented in Dalmatian dogs (6.94 OR to dogs with no cutaneous neoplasias), Basset hounds (3.97 OR dogs with no cutaneous neoplasias). Not surprisingly, cSCC lesions are under-represented color-point breeds, such as Siamese cats. Squamous cell carcinoma arises from epidermal stem cells that have the potential for self-renewal and multi-lineage differentiation. These stem precursors are located in the hair follicle bulge and the basal layer of the interfollicular epidermis. There is also evidence that bone marrow–derived cells may home to the bulge region of the epidermis in response to skin wounding and there differentiate into keratinocyte stem cells. The classic multistep colorectal carcinogenesis model described by Fearon, Vogelstein et al, in 1990, is useful for understanding the progression of sunlight induced skin lesions from the pre-malignant actinic keratosis (AK) stage to cutaneous SCC. The high incidence of cSCC is caused by the mutagenic effects of ultraviolet light (UV) which is intensified by geographic latitude. The mechanism leading to genomic instability in keratinocytes likely results from Ultra-Violet β (UVB)-induced...
inactivation of the p53 protein, which acts as a tumor suppressor gene in skin cancer. It is estimated that approximately 58% of cSCCs harbor UVB signature mutations such as CC:GG to TT:AA and C:G to T:A transitions.

Most patients with primary cSCC have a good to excellent prognosis. Lesions occurring on sun-exposed skin have better prognosis than those occurring in non-sun exposed skin. However, many animals presenting with sSCC have life limiting lesions due to advanced stage at diagnosis or the owner’s inability to financially support extended treatments such as radiation therapy. Surgical excision is the most commonly used modality for curative intent treatments of sSCC. Ear pinna amputation is highly successful in cats as can be excision of the nasal planum. Ventral surface sSCC in dogs is also often successfully managed by surgery, but extensive fields of small lesions may preclude successful resection.

Many local forms of therapy may be applied to individual lesions with varying degrees of success. These types of therapies include cryosurgery, electrochemotherapy, photodynamic therapy, and intraloesional chemotherapy. Topical application of the immunomodulator imiquimod has been successfully applied to superficial lesions in cats, such as on the ear pinna. While dogs have been successfully treated with topical fluorouracil, this treatment is not recommended for cats, as cats are subject to a potentially lethal neurotoxicity with exposure to this agent. Intraloesional fluorouracil or cisplatin chemotherapy in a timed-release collagen gel repositol formulation was successfully used to treat cats, but this gel for suspension is not easily acquired.

Radiation therapy is another successful treatment strategy for sunlight induced sSCC, particularly of the nasal planum in cats. Volume of the sCC was inversely associated with DFI and ST. The 1 year free survival rate was of approximately 60%. Direct application of a radiation source by plesiotherapy (Strontium-90; 50Gy delivered at a depth of 2mm and administered in five fractions over a 10-day period) to small, 2 to 5 cm diameter superficial lesions achieved 87% complete remission with no local recurrences for 2 years. Radiotherapy alone is unfortunately not as effective in dogs with nasal planum SCC, where recurrence is observed in most of the cases within 12-24 months.

Systemic therapy is generally not considered effective in treatment of cSCC, even in cases with lymph node or systemic spread. Some positive responses have been observed through treatment with receptor tyrosine kinase inhibitors which may act both as immunomodulators as well as antiangiogenic agents. Use of RTKI agents targeted against epidermal growth factor receptors (EGFR) are in common and increasing use in human medicine, but treatment with these agents has not yet been described in veterinary medicine.
FELINE LYMPHOMA UPDATE

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Lymphoma has traditionally been the most common malignancy of cats. Before vaccines for FeLV, approximately 50-70% of cats with lymphoma were FeLV positive. Studies of such patients in the 1990's suggest that only 8-14% of lymphoma cats are now FeLV positive, with the contribution of FIV being even smaller. In most recent clinical studies, the median age of lymphoma cats is 9-11 years, with the majority of cats having alimentary site lymphoma.

The immunophenotype of feline lymphomas is rarely determined clinically. However, because FeLV attacks T lymphocytes, T cell tumors have been reported in the anterior mediastinal (thymic) and multicentric forms in about 80% of cases so tested. Small cell T cell lymphomas predominate the alimentary form, which is typically not associated with FeLV infection. However, in the case of gastric lymphoma in cats, B cell disease predominates almost exclusively. Cats are also known to suffer from large granular lymphocyte (LGL) lymphoma, which is notable for the presence of pink granules in the cytoplasm of the lymphocytes. These lymphocytes may be natural killer cells, or may be a subset of cytotoxic T lymphocytes. As they have different lineage ontogeny, they have a dichotomous behavior in that some of these lesions are indolent and while they do not respond well to therapy, they are slow to progress. Other of the LGL lymphomas of cats are rapidly progressive and fatal despite chemotherapy, with a median survival time reported to be 57 days (Vet Comp Oncol 6(2):102-10).

The goal of therapy in LSA is palliation of symptoms by inducing remission, and prolonging the animal's life in comfort. Cure is sometimes achieved in LSA in cats, particularly in cases of localized disease such as in the case of intranasal lymphoma or renal lymphoma. In other cases with indolent or low-grade disease, long-term survival in cats is possible. High-grade lymphoma or lymphoma associated with retroviral disease has a rapidly progressive course and may only respond transiently to therapy. Type of therapy chosen depends largely on the presentation seen.

Local therapy may be used in patients with Stage I disease (localized to one site) with the potential to be curative. Radiation therapy to the local site or surgical resection may be helpful. The cases for which the tumor is locally confined to a single site are rare, however, nasal lymphoma in cats treated with radiation plus 6 months of chemotherapy had a progression free survival duration of 945 days, with approximately 60% of the cats alive and disease free beyond that point. Of the 19 cats treated in this report, 4 (23%) had local recurrence, while 17% had distant metastasis at some time.
Systemic therapy is the most important part of the therapy for high-grade LSA in cats. Several CHOP or COP-based chemotherapy protocols have been published, with most reporting approximately 60-80% of cats obtaining a durable remission of lasting a median of 7-8 months. We employ the standard CHOP-based protocol called the feline version of the University of Wisconsin 25 week protocol. Approximately 20-30% of cats can be expected to live beyond one year. FeLV positive cats tend to be more sensitive to the myelosuppressive side effects. Rescue therapy for relapsed, high-grade lymphoma is typically conducted using a feline version of the MOPP protocol as published in other sources.

Low-grade gastrointestinal lymphoma is the most common presentation seen in older cats. Signs include vomiting, diarrhea, and anorexia with weight loss with cobalamin wasting. A study from Cornell (JAVMA 2008 232(3):405-10) reported the use of oral prednisone and chlorambucil in 41 cats with low grade lymphocytic lymphoma, predominately of the gut. Of these cases, 56% achieved a complete response and 39% a partial response to treatment. Cats that achieved a complete response had a median remission duration of 897 days, while those with a partial response had a median remission duration of 428 days. All had improved clinical signs on therapy. Overall median survival time for the entire group was 704 days. Nutritional support and restoration of B vitamin levels is important for clinical improvement. For cats with large cell high-grade lymphoma of the gastrointestinal tract, we institute therapy with prednisolone and l-asparaginase for 1-3 weeks, along with metronidazole therapy for bacterial overgrowth disease and intense nutritional support, before adding cyclophosphamide and vincristine, in an effort to minimize effects on gut mucosa or motility. Others have reported that mitoxantrone in cat lymphoma is ineffective, but we have managed several cats with alimentary lymphoma on mitoxantrone (5.5 mg/M2 IV infusion over 1 hour) and prednisone therapy with success for several months. Doxorubicin therapy for high-grade disease may also be very helpful.

While it seems contraindicated to apply radiotherapy to the feline intestine, we have successfully rescued out of remission GI lymphoma cats with focal irradiation to the intestine, using 4 gy/fraction dosing on two consecutive days. Cats gained an additional 6-12 months of quality survival after relapse through the addition of focal radiotherapy for GI lymphoma.
Chemotherapy is the treatment of choice for many forms of metastatic cancer. Protocols have traditionally been designed to maximize cytotoxicity of tumor cells by treating with “maximum tolerated doses” (MTD) at the shortest tolerated inter-treatment interval (Skipper 1964). These regimens are also associated with significant side effects and toxicity to normal proliferating cells in healthy tissues. The frequency with which high doses of chemotherapy can be given is limited by how rapidly these normal tissues can recover. During these periods of recovery, cancerous cells are given the opportunity to repair and repopulate. Unfortunately, even when the MTD regimens are efficacious, the responses may be short-lived and the relapsed tumor more aggressive and resistant to future treatment with cytotoxic chemotherapy (Kerbel 1991, Hanahan and others 2000).

Neoangiogenesis is the process by which tumors develop new and expanding growth of blood vessels. Folkman’s hypothesis targets this process for interventional therapy (Folkman 1971), and putative antiangiogenic treatment approaches have received significant attention from the medical community. Several studies have employed combinations of drugs that, when used individually, have exhibited antiangiogenic properties. These protocols have emphasized an approach called low dose metronomic (LDM) therapy, in which administration of chemotherapy drugs targets neovascularization that supports both existing tumors and the emergence of micrometastases. The benefit of targeting normal epithelial cells is that they are under normal cellular control and less likely to develop drug resistance than are the more genetically labile tumor cells. Drug doses necessary to inhibit tumor angiogenesis are significantly lower than those typically used in MTD regimens. The low doses comparatively lessen the toxicity to normal tissues and thus these protocols have the potential to maintain or even increase patient quality of life. In addition to the antiangiogenic effect first noted, it was soon observed that LDM therapy also had an impact to normalize the body’s normal immune response to the tumor, as well as having a modest direct effect on the cancer cells themselves. Thus, LDM therapy is targeted at 3 compartments of the tumor: its vasculature, the infiltrating and circulating immune effector cells, and the cancer cells themselves.

Continuously administered LDM chemotherapy in veterinary medicine is best achieved through use of drugs that are orally bioavailable, such as the alkylating agents cyclophosphamide (CTX), chlorambucil, and lomustine (CCNU). In a seminal study of metronomic therapy, Browder and colleagues (2000) revealed that when CTX was administered at MTD, endothelial cells within various tumor types were the first to undergo apoptosis. However, this antiangiogenic effect did not translate into benefit as the vasculature was repaired during the two to three week interval between treatment cycles. Browder
further showed that when CTX was given at lower doses and at an increased frequency, the antiangiogenic and antitumor effects were impressive even in tumors comprised of cancer cells that were resistant to CTX. Recent studies by Dr. Barb Biller of Colorado State University indicate that low doses of cyclophosphamide (ie 15 mg/m2 PO daily as reformulated capsules) can re-balance the immune system by decreasing levels of regulatory T lymphocytes (T-regs), which act as “suppressor T’s”. In dogs with high levels of CD8 cytotoxic T lymphocytes compared to T-regs, survival and disease free interval was statistically prolonged in canine osteosarcoma patients when compared to dogs with a decreased CD8/T-reg ratio.

Multiple reports indicate that cyclooxygenase-2 (COX-2) is up-regulated in a variety of human and canine tumors. *In vivo* studies in mice and rats suggest that COX-2-derived prostaglandins play a major role in the proliferation of new vascular-associated cells during angiogenesis. Although the effects of selective COX-2 inhibitors on tumor angiogenesis in dogs has not been extensively studied, there is some evidence that inhibition of cyclooxygenase enzymes by nonsteroidal anti-inflammatory drugs (NSAIDs) may interfere with endothelial cell tube formation and vascular endothelial growth factor (VEGF) production (Lana and others 2007).

The receptor tyrosine kinase inhibitors are orally available agents that block angiogenesis through their promiscuous inhibition of critical receptors such as VEGFR and PDGFR. Many clinicians in the US are adding toceranib or masitinib to LDM style protocols. Most recently it has been demonstrated that toceranib has the capacity to normalize immune responses to tumor as well as to inhibit VEGFR signaling.

Pioglitazone (Actos; Takeda Pharmaceuticals) and rosiglitazone (Avandia; GlaxoSmithKline) are thiazolidinediones (TZD) that essentially bind to the peroxisome proliferator-activated receptor γ (PPARγ), which belongs to the lipid-ligand-regulated nuclear hormone transcription factor superfamily. Research by Berger and others (2002) has revealed that activation of PPARγ ligands block the cell cycle and cause differentiation of primary liposarcoma cells in culture. Rosiglitazone has been shown to inhibit angiogenesis in a variety of tumors by causing a decrease in VEGF receptor expression by endothelial cells, as well as upregulation of CD36 receptor expression. CD36 is the receptor for antiangiogenic thrombospondin 1.

One of the most critical advantages of LDM style therapy is that it can be highly cost-effective, as no injectable drugs are typically employed and the dose ranges used are modest to moderate. Dose limiting toxicities are not anticipated from these regimes, although occasional adverse effects can be anticipated from any drug treatment. Thus, veterinary clinicians have begun using metronomic combination chemotherapy using a NSAID drug such as piroxicam, daracoxib, carprofen, or meloxicam, along with continuous low dose cyclophosphamide, or other alkylating agent, by mouth. Some protocols are supplemented with other potentially therapeutic agents such as toceranib, which is a VEGFR2 inhibitor, or doxycycline. These studies are ongoing, but the impact of this approach is also being
promoted because of the potential for cost-effective anticancer therapy. We will discuss several protocols and preliminary published results of their use.
Oral melanomas in dogs have a poor prognosis, with only about 25% of patients historically surviving one year after treatment. Local-regional tumor recurrence and systemic metastasis contribute to treatment failure. Therefore, even if complete surgical excision of the primary tumor is possible, tumor spread via metastasis remains a problem. A multidisciplinary approach to treatment, including surgery, radiotherapy, chemotherapy, and immunomodulatory therapy may enhance survival.

Surgical excision is indicated when the tumor can be completely excised without the result compromising the quality of life. Surgical resection with 1-2 cm margins is recommended where feasible. There is a definite survival advantage when more radical surgical approaches are employed, with 480 day median survival for aggressive surgery vs. 74 day median survival for more conservative resection reported in one study.

Mandibular melanoma has a more favorable prognosis than maxillary disease, possible because of the improved potential for radical mandibulectomy as opposed to maxillectomy. Regional lymph nodes should be excised at the time of primary tumor resection. Microscopic evidence of metastasis may be detected even in lymph nodes of normal size. In a retrospective study of lymph nodes resected from 100 dogs with oral melanoma, 47% had nodal metastasis on histologic evaluation. Significantly, while 70% of these node positive dogs had enlarged lymph nodes, 30% of dogs with nodal metastasis on histology had normal lymph node size on physical examination. Thus, while enlarged lymph nodes often indicate metastasis, normal lymph nodes on palpation cannot rule it out.

Radiation - The use of radiation is limited to an adjunctive role, because most melanomas are relatively resistant to radiotherapy, and radiation therapy to the local tumor bed does not address the life-limiting problem of systemic spread. There are inherent advantages in using radiotherapy in the head and neck region with its anatomical complexity and cranial nerves and other vital structures in high concentration. Aggressive surgery can result in functional as well as cosmetic abnormalities. While most veterinary patients can compensate for loss of function and are not bothered by cosmetic alterations, these complications do represent a significant barrier to some clients. A benefit of radiotherapy is that regional lymph nodes can also be irradiated. Radiation therapy protocols for melanoma typically involve coarse fraction delivery (hypofractionation), such as 8 Gy per fraction delivered in 3 or 4 doses. This type of protocol was reported to result in an overall response of 83% (complete response: 53%, partial response: 30%, no response or stable disease: 17%). The same protocol induced remission in 3/5 cats treated for oral melanoma and resulted in a median survival time of 146 days. A variety of other protocol schemes have been reported, including 36 Gy delivered in 4
fractions, 30 Gy delivered in 3 fractions, and 45 Gy or more delivered in 12-19 fractions of 2-4 Gy per fraction. In a large case series reported from NCSU, 140 dogs radiated with one of the 3 previously described fractionation schemes showed no superior method of radiation. Dogs treated with radiation therapy had a median time to first event (recurrence or metastasis) of 5 months and median survival of 7 months.

**Chemotherapy** for metastatic disease or as an adjunct to surgery and radiation therapy has largely been through the use of dacarbazine in veterinary oncology, although evidence of response to systemic carboplatin and lomustine have also been noted anecdotally and in limited case series. Melanomas have been found to express Cox-2 and may therefore respond to this signaling as a growth factor. Adjunctive treatment with a Cox-2 inhibitor such as piroxicam or newer more selective coxibs is worthy of additional investigation. Additionally, evidence of efficacy of a combination of cisplatin (50 mg/M2 IV with a 6 hour saline diuresis) plus piroxicam (0.3 mg/kg daily PO) induced responses in dogs treated for oral melanoma. Renal toxicity was dose limiting and requires careful monitoring.

**Immune, Vaccination, and Gene Therapy** - Long-term survival of dogs with advanced malignant melanoma was achieved after DNA vaccination with xenogeneic human tyrosinase antigen, available under limited license in the United States from Meriel (Oncept®). This xenogeneic vaccine contains human DNA for the gene tyrosinase, which is highly expressed in melanocytes as part of the production of melanin pigment. The gene is under the control of a strong cytomegalovirus (CMV) promoter, which results in production of the human protein in canine muscle. The vaccine is introduced to muscle by use of a needle-less bioinjector system. Once the dog begins to produce the human protein, the canine immune system recognizes the human tyrosinase enzyme and is hopefully sufficiently potent to break self-tolerance to eradicate remaining microscopic (or in some cases even macroscopic) melanoma tumor burden in the dog. The vaccine is administered on a 2-week basis for 4 treatments, then as booster injections every 6 months. Responses have been seen even in dogs with transient tumor progression. Optimally, dogs should have the tumor burden reduced to T0 by surgery and/or radiation therapy prior to vaccination. In the phase one trial, median survival for 9 dogs treated was 389 days, with complete responses reported and greater that 588-day survival for one dog with bulky non-resectable disease. Dogs that demonstrated antigen specific antibody responses were more likely to have positive responses clinically. Expanded trials have been reported that demonstrate improved disease free interval and survival over historical controls. Other immune approaches under study for canine oral melanoma include treatment with allogeneic and autologous tumor cell vaccines, gene therapy, cytokines, and antibodies. The rationale for tumor cell vaccines is based on the idea that attenuated transfected tumor cells may serve as an antigen source and a vehicle to deliver immunostimulatory cytokines concurrently. Most recently, promising results were noted in a trial using an adenovirus vectored CD40 stimulatory molecule as the active agent. Further tests of this approach are ongoing in Europe.
Ocular neoplasia is characterized based on species, location affected and whether it is a primary or secondary tumor. The behavior of ocular neoplasia varies significantly based on these criteria. For example, an iris melanoma is generally considered benign in the dog, but may be malignant in the cat. A canine ocular melanoma involving the limbus or anterior uvea is benign while one originating from the bulbar or palpebral conjunctiva behaves in an aggressive and malignant fashion. In general, ocular neoplasms are described as extraocular (eyelids, third eyelid, conjunctiva), corneal, intraocular and orbital.

Adnexal/Corneal

Most adnexal neoplasms of the canine eyelids are benign. They include cutaneous histiocytoma, melanoma, meibomian adenoma, epitheliomas and basal cell tumors. Mast cell neoplasms are also seen and can be more aggressive both locally and can metastasize. Neoplasia of the feline eyelid is less common, but typically more aggressive than in the canine and includes squamous cell carcinoma, mast cell and fibrosarcoma. Treatment for both species generally includes surgical excision, but adjunctive therapy may be required especially in the cat. Cryosurgery is also a consideration for smaller, benign eyelid masses. Interestingly, it is noted that even with incomplete excision, the prognosis for mast cell tumors of the feline eyelid remains excellent while this is not the case in the dog.

Primary conjunctival neoplasms, in both the dog and cat, often behave in an aggressive fashion with local recurrence and distance metastasis not uncommon. Melanomas, squamous cell carcinomas, mast cell tumors, lymphosarcoma and hemangiomas/hemangiosarcomas are all seen to involve or arise from the conjunctiva. Neoplasms of the third eyelid may include adenoma/adenocarcinoma of the gland, lymphosarcoma and squamous cell carcinoma. Local excision, enucleation or exenteration may be indicated depending on the location, size and tumor type. Systemic evaluation for metastasis is advised.

Limbal melanoma (melanocytoma) arising from the corneoscleral junction are seen in both dogs and cats. They are typically benign with local excision indicated if it is enlarging and often curative. In the dog, limbal melanocytomas are often seen in younger animals and have a breed predilection with German shepherds and shepherd-like breeds more commonly affected.

The most common corneal neoplasm is a squamous cell carcinoma. In the dog it is most frequently secondary to chronic irritation seen with keratoconjunctivitis sicca and may be exacerbated by longstanding therapy with topical cyclosporine or tacrolimus. In addition, dermoids, papillomas, hemangiomas and lymphosarcoma may involve the cornea.
**Intraocular**

Intraocular tumors mostly commonly arise from or involve the vascular tunic, the uvea. Common primary uveal neoplasms include melanoma, adenoma and adenocarcinoma. Additional primary intraocular tumors may include medulloepitheliomas, feline spindle cell sarcomas and schwannomas. Tumors arising from the optic nerve include astrocytomas or gliomas.

The most common metastatic tumors are lymphoma and histiocytic sarcoma, but any malignant tumor may have an affinity for the eye as a result of the extensive vascular supply to the eye. In general, metastatic neoplasms tend to elicit more secondary uveitis, hyphema and glaucoma than do primary intraocular neoplasms.

**Orbital**

Neoplasia of the orbit may present for exophthalmos, globe deviation, pain, periorbital swelling and possible vision loss. Orbital tumors can be primary, arise by extension from adjacent structures (nasal, sinus) or be metastatic. Primary orbital tumors include meningiomas, lipoma/liposarcoma and glandular tumors of the lacrimal and salivary glands. Extension of carcinomas, sarcomas and other tumors arising from the nasal and sinus tissues is common with the ocular involvement often the first presenting complaint. Lymphosarcoma may involve the orbit unilaterally or bilaterally.

**References**


RECEPTOR TYROSINE KINASE INHIBITORS IN VETERINARY MEDICINE

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While a variety of pathways have been established as anticancer treatment targets, signaling molecules in the receptor tyrosine kinase class seem to be the closest to providing a window to clinical applicability. These agents can target a variety of the 400+ individual kinases, and much clinical exploration will be carried out in the years to come.

Masitinib (AB Science) has been available for clinical use in Europe since 2008 and was granted limited license in the United States in 2010. The primary target for Masitinib is the tyrosine kinase receptor c-kit, whose ligand is stem cell factor (SCF). Activation of this receptor is pivotal in regulating the growth, differentiation, adhesion, motility and cell death of mast cells. An estimated 30% of canine malignant mast cells express a mutated isoform of c-kit that leads to constitutive activation of the receptor in the absence of ligand binding. Masitinib acts by potently inhibiting the phosphorylation of various isoforms of c-kit including both wild and mutant types (most common being at exons 8, 9 or 11), blocking the intracellular signals driving tumor progression. It also has affinity for additional receptors such as platelet derived growth factor (PDGFR) and the cytoplasmic kinases Lyn, Fyn and Lck. Masitinib is labeled for oral use; excretion is predominately through the feces, with the parent compound accounting for nearly 50% of the material excreted. Gastrointestinal toxicity including vomiting, diarrhea and loss of appetite are noted commonly, but are typically mild and self-limiting. A proteinuria syndrome has been observed which can be dose-limiting, with recommendations to discontinue therapy if severe hypoalbuminemia (<0.75 of normal) is noted. Although rare, hemolytic anemia has been documented. Other rare toxicities include elevation of liver transaminases and/or neutropenia. Drugs that interact with the same CYP450 isoenzymes (2C9, 2D6 and 3A4) as Masinitib should be avoided if possible. Masitinib is indicated for use in the treatment of non-resectable and metastatic canine mast cell neoplasia, particularly those tumors carrying a mutation of c-Kit. It is also in clinical trials for treatment of canine atopic dermatitis and reactive airway disease. Several additional clinical trials are underway to evaluate efficacy in canine T-cell lymphoma, canine melanoma and canine hemangiosarcoma. Exploration of use in feline cancers is underway also.

Toceranib was developed by Pfizer to target the tyrosine kinase receptors c-Kit, VEGF and PDGF. Toceranib (Palladia, SU11654) is the first dog-specific anticancer drug licensed in the U.S. It was made commercially available in the United States in 2010. Toceranib interferes with phosphorylation of various tyrosine kinase receptors, including c-Kit, VEGF-R, PDGF-R, and FLT3. It blocks phosphorylation by directly interfering with the ATP binding site for kinase activity in the intracellular domain of the receptor. This leads to...
cessation of intracellular signaling for growth and differentiation and cell death occurs via cell cycle arrest and apoptosis. Toceranib is reported to have significant anti-angiogenic properties as well. Toceranib comes as a tablet and is widely distributed, reaching maximum serum concentration in about 4-6 hours after oral administration. Excretion occurs through the vomit, feces and urine. Gastrointestinal toxicity, including diarrhea, vomiting, weight loss, and anorexia are possible. Diarrhea is observed most commonly (about 46% of patients) and can be dose-limiting and fatal if untreated. Myelosuppression, with neutropenia most commonly seen, is generally mild. Rare toxicity includes elevation of ALT, hypoalbuminemia and musculoskeletal disease. Patients can experience severe signs related to degranulation of mast cell tumors during treatment. Toceranib is US licensed for the treatment of Patnaik grade II or III, recurrent, cutaneous mast cell tumors with or without regional lymph node involvement in dogs. Newly reported studies demonstrate potential efficacy against canine soft tissue sarcoma, mammary carcinoma, anal sac and thyroid carcinomas, multiple myeloma, and osteosarcoma. It is not recommended for patients with visceral mast cell disease and should not be used in patients with preexisting diarrhea or gastrointestinal bleeding. Its use in combination with traditional cytotoxic drugs, NSAIDS, and corticosteroids should be approached with caution.

Concurrent medications are recommended with toceranib due to significant risk of gastrointestinal toxicity. The current recommendations from Dr. Cheryl London, the key developer of this drug in veterinary medicine, is to treat dogs that have minimal residual mast cell tumor burden, due to the risk for significant degranulation effect. It is recommended that the starting dose be 2.5 mg/kg given on an every other day basis, or even on a MWF basis, rather than the 3.25 mg/kg dose given daily as per the manufacturer’s recommendations. The lower dose has similar biologic activity to what is seen with the higher dose, but the toxicity profile is much more tolerable. Additionally, Dr. London recommends premedication for at least 5 days with corticosteroids, antihistamines of H1 and H2 class, and potentially even a proton pump blocker (omeprazole). Prednisone is recommended to be given on the off day of toceranib administration. Loperamide is the currently recommended agent for managing diarrhea induced by toceranib, and it should be administered on days of toceranib administration as needed for diarrhea. Perforating gastric ulcers and even death of some patients has been seen, so clients should be advised of the GI toxicity risk, and thus be on the alert for any level of GI signs, including anorexia as a minimum, and also vomiting and diarrhea. In face of GI signs drug administration should be halted (a drug holiday) and gastroprotectants should be used until all signs resolve. At that time, toceranib therapy can be re instituted with a dose reduction and/or increased interval between doses. These modifications have resulted in a much more favorable toxicity profile for the drug.

In addition to the two described RTKIs, the human drug imatinib (Gleevec) has activity against canine mast cell disease. Newer kinase inhibitors from the human side, such as those against receptors EGFR, MET, MEK, SRC and many others, are under study for use in canine and feline malignancies.
The majority of abnormalities associated with canine eyelid position begin with a problem of length, specifically macroblepharon. Failure to address the issue of length when correcting entropion, ectropion or their combination will often result in a less than satisfactory result and possible failure. As a surgeon, I have never surgically corrected abnormalities of eyelid position without first measuring and correcting the associated problem of macroblepharon. In general, most canine eyelids can be shortened to 24-26 mm using the technique of lateral canthoplasty and then the residual eyelid corrected for position. Remember, the eyelids are there to serve and protect the cornea and the medial to lateral length of the canine cornea is approximately 16 mm regardless of breed.

Abnormalities of position will include entropion, ectropion and a combination of both. First, measure the length of the eyelids using Jameson calipers. Perform a lateral canthoplasty to shorten the eyelids to the appropriate length and then for entropion a Modified-Hotz celsus may be performed to correct the remaining in-rolling of the upper and/or lower eyelids. For simple ectropion, the lateral canthoplasty alone may be sufficient to correct mild cases. For more severe ectropion, additional wedge-resection or other techniques may be required. For entropion/trichiasis of the medial canthus, as seen in the Pug, a medial canthoplasty may be indicated. While similar to a lateral canthoplasty, care must be taken to avoid trauma to the nasolacrimal ducts.

When suturing eyelids, the smallest suture indicated should be used. This is typically 6-0 to 7-0 suture. For the deep layer, an absorbable suture such as polygalactin may be used. For the skin, the author prefers a monofilament polypropylene type suture as these are less reactive and will result in less inflammation and a better outcome. Sutures should be kept clean using a warm, moist compress and an E-collar worn.
In addition to abnormalities of position, abnormalities of hair such as distichia, ectopic cilia and trichiasis are also common. Depending on the severity these may or may not require treatment. Of these, ectopic cilia is the most common to require treatment and is more common in certain breeds such as the Shih Tzu. Treatment should be directed at not only removing the hair, but also destroying the hair follicle. This can be done using surgical excision, cryosurgery or laser ablation.

Eyelid agenesis is seen as a congenital abnormality in the cat. It most commonly affects the superior temporal eyelid and treatment is indicated if the health of the cornea is compromised. A lip to eyelid transposition is the most effective surgical treatment.

Eyelid neoplasia in the canine is most often benign while in the cat eyelid neoplasia may be more aggressive and can undergo metastasis. The most common eyelid neoplasms in the dog include Meibomian gland adenomas, melanomas, papillomas, mast cell tumors, histiocytomas and basal cell tumors. In the cat, mast cell tumors, fibrosarcomas and squamous cell carcinomas are most common. In general, up to 1/3 of the eyelid may be removed and a primary closure performed. This is provided the lesion involves the 12 or 6 o’clock positions. If a primary closure cannot be performed a grafting procedure such as an H-plasty, rotational graft, lip-eyelid or other such procedure may be considered.

Eyelid Wedge Excision

The most common abnormality of the 3rd eyelid is prolapse of the gland of the nictitans. It is important to remember that NO MATTER what you do, these eyes are at increased risk for KCS. The greatest risk would be to excise the gland and this is contraindicated. The least risk for KCS would be surgical replacement with no therapy being the middle risk group. There are several techniques for replacement and of those I have tried, the pocket imbrication technique works the best for me.
Scroll cartilage is also seen in the 3rd eyelid of large breed dogs or secondary to chronic prolapse of the nictitans gland. A new technique using thermal cautery to correct the scrolled cartilage appears to be both effective and simple.

References


Corneal disease is common in both dogs and cats and can be primary or secondary to other ophthalmic or systemic disease. Corneal disease may result in opacification, vascularization, pain, ulceration, pigmentation or perforation. Owners will often present animals early in the course of corneal disease as the clinical signs of epiphora, blepharospasm, photophobia, pawing and opacification are readily apparent. Despite this, corneal disease may progress rapidly and be advanced at the time of presentation, requiring immediate and aggressive medical or surgical intervention.

When presented with ulcerative keratitis, the clinician must, if possible, identify the etiology and if still present, eliminate it. This would include foreign bodies, eyelid positional abnormalities, abnormal hairs, blink and tear abnormalities and infectious causes. A complete ophthalmic examination and possibly corneal cytology and culture are indicated.

Corneal ulcers should be classified according to depth, size, etiology, presence or absence of infection, and collagenase activity. Culture and sensitivity, STT, cytology, fluorescein stain retention, and complete anterior segment examination should be considered as part of a routine examination in animals with a corneal ulcer. Most corneal ulcers are superficial and heal rapidly without complication. Medical therapy will prevent or eliminate infection, alleviate discomfort and facilitate healing. Surgical therapy should be considered for a stromal abscess or ulcers that fail to heal, worsen despite treatment or are deep or melting at initial presentation. Descemetoceles and perforated corneal ulcers are considered surgical emergencies. Surgical treatment of choice varies according to size and depth of the corneal defect.

Medical therapy for ulcerative keratitis may include topical application of artificial tears, broad spectrum antibiotics, mydriatic-cycloplegics and antiinflammatory/immune modulating drugs such as non-steroidal antiinflammatories and cyclosporin. The antibiotic of choice will often depend on the severity of the disease, cytology and culture results, cost and clinician preference. Systemic medications are of limited value for treatment of non-penetrating corneal disease, but are occasionally used to supplement topical therapy. The frequency of administration of topical medications varies according to the severity of the disease ranging from every 2-8 hours. When administering multiple topical medications solutions should be administered before ointments and medications should be spaced 5 minutes apart.

Surgical management of corneal disease includes a superficial linear keratotomy/diamond burr for refractory indolent ulcers; keratectomy for dermoids, neoplasia, sequestration and infected/necrotic ulcers; laceration repair; conjunctival grafts, corneoconjunctival grafts and
other corneal transplantation techniques. The ophthalmic surgeon should be fully versed in microsurgical techniques and utilize appropriate surgical instrumentation, suture material and magnification to maximize the opportunity for a successful outcome. In addition, the clinician must be familiar with corneal anatomy and physiology and with specific adjunctive medical therapy as indicated by the inciting cause and the surgical procedure performed.

Prior to surgical correction of corneal disease, a complete ophthalmic examination is essential. The presence of associate or exacerbating adnexal or intraocular disease should be identified and managed prior to or at the time of corneal surgery. Failure to correct problems such as blepharitis, entropion, keratoconjunctivitis sicca (KCS), distichia or other adnexal abnormalities may result in failure of corneal surgery regardless of how well it is performed.

To perform corneal surgery the animal must be under general anesthesia. For more involved corneal surgery, use of a non-depolarizing neuromuscular blocking agent intravenously may be required. If needed, one or more stay sutures placed in the episclera at the inferior-medial aspect of the globe can be used to rotate the globe up while rotating the third eyelid down. Head positioning is essential. The animal is placed in lateral or dorsal recumbency and the head positioned such that the cornea is parallel with the table and the eye looking towards the ceiling. A vacuum pillow will facilitate this positioning and ensure immobilization during surgery. An eyelid speculum is used to retract the eyelids and provide exposure. If greater exposure of the cornea is required, a lateral canthotomy can be performed to enlarge the palpebral fissure. Magnification in the form of surgical loupes will facilitate precise incisions, delicate tissue handling and accurate wound closure. Appropriate magnification for corneal procedures ranges from 2.5-10 X. Surgical loupes are less expensive and may provide adequate magnification (2.5-5.0X) for routine corneal surgery. Throughout any corneal surgical procedure irrigation of the cornea to prevent drying is essential. This will preserve the corneal epithelium, improve tissue handling and visualization and result in less postoperative complications. Suture material is generally 7-0 to 9-0 in size and most often absorbable.

References


CATARACT – what can I do?
„NOT ALL CATARACTS ARE THE SAME“

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The lens is normally transparent and devoid of blood vessels. It is biconvex body with an anterior surface that is flatter or less curved than posterior surface. The centres of the surface are called anterior and posterior poles. Rounded circumference is the equator, which has numerous irregularities where zonular fibers attach. Posterior aspect is in contact with the vitreous and depression in the vitreous is called the hyaloid fossa. Opacification of the lens, cataract, may occur, however, either because of malformation or caused by cataractogenous factors later in life. Cataract is in ophthalmic terminology an opacification of the lens and/or lens capsule. The opacities may be of varying sizes, shapes, location within lens, etiology, age of onset and rate of progression.

The hollow lens vesicle is filled through elongation of the posterior epithelial cells. These primary fibres, developed in foetal life, form the nucleus of the lens. The anterior lens epithelial cells stay short. Towards the lens equator the lens epithelial cells elongate and develop into fibres, which form the future lens cortex. This process continues throughout the whole life of the animal. Thus, new fibres are constantly formed in the periphery, pushing the older fibres towards the middle of the lens. This, together in reduction of water content and aggregation of proteins in the lens results in a bluish appearance of the lens, nuclear sclerosis. Nuclear sclerosis is a normal finding in old dogs and should not be confused with cataract. Advanced nuclear sclerosis may appear similar to cataract, and in fact, the two are frequently confused by owners and practitioners. Mydriatics and retroillumination can help in differentiating between the two entities. In most animals, except for the most severe cases, the effect of nuclear sclerosis on vision is minimal, and the fundus can be readily visualized.

Examination of the lens

Dark room is absolutely essential for lens examination. For full examination of the lens a mydriatic is needed. Tropicamide is instilled at least 20 minutes before examination to allow full pupil dilation. A simple examination of the lens can be performed with a focal light source and a headband loupe; more sophisticated instruments include the slit-lamp biomicroscope. The light is directed directly into the eye to allow the reflex from the fundus (retroillumination). Opacities may be seen as darker areas through the pupil. Directing the light at an angle allows localization of the opacities.
Normal findings

The suture lines of the lens, shaped as a Y at the anterior pole and opposite Y at the posterior pole can often be observed as faint lines. So-called “arrowhead” opacities may be seen in the peripheral suture lines, especially in young dogs. These arrowhead opacities often disappear with age. Small remnants of the hyaloid artery may often be observed as normal variations. A small hyaloid remnant may often be seen attached to the posterior lens capsule and extending into the vitreous in an otherwise healthy eye.

In older animals, nuclear sclerosis is the result of lens growth throughout life, decreased water content and increased lens density, which must be distinguished from cataract. In nuclear sclerosis, there is reflection from the whole fundus in retroillumination, while dark opacities are seen in cataract.

Normally, no opacities apart from what is mentioned here shall be seen when light is directed straight through the lens.

Cataract

As I mentioned earlier - cataract is in ophtho-terminology an opacification of the lens and/or lens capsule. Cataracts may be classified according to cause. The most common cause of cataracts in many dog breeds is inheritance. Other causes are metabolic, nutritional, traumatic, toxic and developmental or secondary to other ocular diseases. Ophthalmologists can classify cataracts according to the location of the initial opacity. We have nuclear, cortical, subcapsular cataract and we can decide cause of cataracts depends on initial location. Another view is age of onset. In many breeds inherited cataracts are characterized by typical age of onset.

Prevalence of cataracts in mixed breed dogs, which are presumably not affected by hereditary cataracts, is 1,61%, in purebred dogs is higher (2,42%), thanks to improved training and diagnostic techniques in veterinary ophthalmology and to increased popularity of purebred population.

In practice, the stage and type are the most important criteria. The stages of cataract development:

* **Incipient cataract** describes focal opacification(s) of the lens and/or its capsule. Vision is not impaired. This cataract may or may not progress.

* **Immature cataract.** The opacity is more or less diffuse, but the fundus can still be examined. Vision may or may not be impaired. The changes are mostly progressive.

* **Mature cataract.** The fundus cannot be inspected, as the opacification is total and dense. Vision is severely impaired.

* **Hypermature cataract.** Dissolving of the cataract may occasionally occur. The content of the lens capsule is more or less liquefied. Lens protein can be resorbed, leading to shrinkage
of the lens with wrinkling of the capsule. The nucleus will dissolve to a lesser extent, and may migrate inferiorly in the capsular bag to form what is termed a Morgagnian cataract.

If a cataract is present before the 6\textsuperscript{th} to 8\textsuperscript{th} week of life, it is considered 	extit{congenital}. Cataracts developing after the 8\textsuperscript{th} week are termed 	extit{developmental} (or juvenile). 	extit{Senile} cataracts occur in aged animals, but should not be confused with 	extit{nuclear sclerosis}, which is a normal ageing process of the lens.

**Congenital cataract**

Congenital developmental abnormalities of the lens often occur in combination with other malformations of the eye. The most common include: 	extit{Microphakia} – inadequate (small) size of the lens. Elongated ciliary processes will be seen surrounding the lens, and the lens borders are clearly visible when the pupil is dilated. The condition may be breed related, as in the Miniature Schnauzer where it is associated with congenital cataract. 	extit{Lenticonus/lentiglobus} - a thinning of the lens capsule permitting the cortex to bulge, causing a conical malformation at the anterior or, most commonly, the posterior pole. Lentiglobus is more severe than lenticonus.

**Congenital hereditary cataract** is often dense and slowly progressing. It may occur in combination with other congenital eye abnormalities, such as microphthalmia, retinal dysplasia, PPM, posterior lenticonus/lentiglobus and PHTVL/PHPV.

Apart from the cataract in the Miniature Schnauzer, which is inherited autosomal recessively, the mode of inheritance has not been established. A recessive model has been suggested for congenital cataract in the miniature schnauzer, the Afghan hound, the Bichon Frisé and the American cocker spaniel, while in the golden retriever cataract is suggested to be inherited by a dominant gene. Very few breeds have been investigated regarding modes of inheritance. Our knowledge regarding modes of inheritance is restricted, thus breeding recommendations also usually are limited to recommending not to breed affected dogs.

It is important to note that not all congenital bilateral cataracts are inherited.

**Hereditary cataract**

Hereditary cataract may be primary, not associated with other eye abnormalities, or occur secondary to other ocular conditions. Hereditary cataracts have been described in many breeds of dogs, and the list is continuously increasing. According to the genetic material in different countries, the incidence of hereditary cataracts within a breed may differ significantly. Hereditary cataracts are far rarer in cats, but are suspected to occur in the Persian and Himalayan.

When the ophthalmologist diagnoses cataract in a dog examined for hereditary eye diseases, the important issue is to determine if the cataract represents an inherited disease or not. ECVO hereditary committee defined those criteria.
In many breeds, posterior polar cataract is the most common manifestation of hereditary cataract. However, there are breed differences as to localization of initial cataract changes within the lens. Initial cataract changes in the flat coated retriever may be seen in the anterior suture lines, while cataract in the Afghan hound usually starts at the equator, in the periphery of the lens. Late developing cataract in the Boston terrier presents as discrete linear or wedge-like anterior subcapsular or outer cortical opacities extending in a radial fashion from the equator to the centre of the lens. The fact that some cataract changes initially appear in the periphery emphasizes that pupil dilation is necessary for a thorough examination of the lens.

**Traumatic cataract**

Traumatic cataract can develop as a result of a deep stab wound by for instance a cat claw. If the perforated lens capsule heals quickly, the damage can be limited to a local non-progressive cataract. Blunt trauma or larger wounds may cause more extended changes, progressing to complete cataracts. Tearing of the lens capsule results in leakage of lens proteins into the anterior chamber with subsequent uveitis.

**Toxic cataract**

Several toxic substances can cause cataract. These include antimitotic agents, enzyme inhibitors and certain metals. Cataract formation after long-term therapy with ketoconazole has also been described. A brand of commercial milk replacement produced cataracts in zoo animals.

**Cataract secondary to other ocular diseases**

In a number of other eye diseases, cataract can develop secondarily. Progressive retinal atrophy (PRA) often results in secondary cataract obscuring the primary disease. Questioning of the owner about onset, vision in daylight and under reduced lightning conditions, as well as the age and the breed of the dog is of essence to establish a diagnosis. ERG should always be performed before cataract surgery when primary retinal disease is suspected.

Uveitis, especially in the cat, frequently leads to cataract formation, as do lens luxation and glaucoma. These cataracts are caused by an altered composition of the aqueous humour, which is responsible for lens nutrition.

**Cataract secondary to systemic diseases**

Diabetes mellitus is a common cause of cataracts in the dog, and most diabetic dogs eventually develop lens changes. The cataracts are bilateral, very rapidly progressing and involve the whole lens. Typical findings in diabetic cataracts are broad and clearly visible suture lines ("water-cleft" formation). The cause of cataract has been considered to be an increase in glucose in the aqueous. The excess glucose is metabolised via the aldose reductase and sorbitol pathway resulting in increased concentration of sorbitol. Sorbitol acts as an osmotic agent drawing water into the lens cells, thus causing swelling of the fibres and loss of transparency. Diabetic cataracts are uncommon in the cat, although cases have been reported in the literature.
Treatment of cataract

No effective medical treatment for cataract has been successful. Surgical treatment with lens extraction is commonly performed. The general condition of the patient as to health and behaviour should be considered. Cataracts secondary to other eye diseases compromising vision should not be treated surgically unless the lens changes cause problems that can be relieved in this way. There is the most used technique for cataract surgery: phacoemulsification, when the lens material is fragmented by ultrasound and aspirated. Cataract surgery should be left to referral veterinarians with special interest in ophthalmology and experience in lens extractions.
Abnormalities of the anterior segment most commonly result in redness, pain, cloudiness and loss of vision. The most common include inflammatory diseases of the iris and ciliary body (anterior uveitis), elevated intraocular pressure (glaucoma) and opacity of the lens (cataract).

**Anterior Uveitis**

The clinical signs of anterior uveitis include miosis, aqueous flare, hypotony, keratic precipitates, redness, photophobia and deep corneal vascularization. When diagnosed, it is essential to then decide if the uveitis is from a primary ocular etiology or an ocular manifestation of a systemic disease. There are 4 primary ocular reasons for anterior uveitis. They are corneal ulceration, cataract with lens-induced uveitis, ocular trauma or a primary intraocular neoplasia. If one of these is not the etiology then the clinician must consider a systemic etiology. Systemic etiologies typically include idiopathic, immune-mediated, metastatic neoplasia (lymphosarcoma most common) and infectious causes. In general, approximately 50% of case will fall into the idiopathic/immune group, 25% into the neoplastic group and 25% into the infectious group. The variability is in the infectious group where the type and likelihood of an infectious etiology will vary by geographic location and time of the year. In addition the infectious etiologies differ between dog and cat. In the canine – tick associated disease (erlichia, RMSF, Lyme), mycotic infections, prothecosis, leishmania, bacteremia and septicemias are most common while in the cat FeLV, FIV, Toxoplasmosis, FIP, cryptococcosis and Bartonella are most common. Keep in mind, in the cat these are not mutually exclusive diseases and it is common for a cat to be infected with multiple etiologies.

When presented with a case of anterior uveitis of a non-ocular etiology the clinician must obtain a detailed history, perform a complete physical examination and consider blood work for a complete blood count, serum chemistry and serologic testing. In addition a urinalysis, chest radiographs, abdominal ultrasound, fine-needle aspirate, cytology and histology may also be indicated. Treatment of anterior uveitis will depend on the primary etiology which must be diagnosed, treated and eliminated. In addition, topical mydriatics and anti-inflammatory therapy and possible systemic anti-inflammatory therapy may also be indicated. Failure to control anterior uveitis may result in cataracts, glaucoma, phthisis bulbi, synechia, corneal edema and blindness.
Glaucoma

Glaucoma is an increase in intraocular pressure (IOP) incompatible with the health of the eye. In general, using a Tonopen or Tonovet most dogs have an IOP <20 mmHg. The Tonovet will tend to read slightly higher than the Tonopen. For predisposed breeds with an IOP >20 mmHg treatment and possible referral should be considered. While it can be debated, I do advise annual determination of the IOP in all predisposed breeds after the age of 3-4 years. It is also essential to determine the IOP in all eyes with anisocoria, fixed and dilated pupils, uveitis, all red eyes, cloudy eyes, painful eyes, blind eyes, enlarged eyes, all eyes with a diagnosis of glaucoma on therapy and the contralateral eye in all dogs with primary glaucoma in the affected eye. It is therefore essential that all practices have access to a working, reliable tonometer and know how to use it.

Once diagnosed, glaucoma is divided into primary and secondary and acute and chronic groups. Of these, acute primary glaucoma is the most likely to be treated and retain vision. Treatment will include both medical and surgical management. Of the medical treatment, topical prostaglandins, topical carbonic anhydrase inhibitors and oral carbonic anhydrase inhibitors are the only medications with significant efficacy in the dog. Surgical options for a visual eye will include diode laser therapy, preferably endolaser and/or implantation of a drainage device. Chronic glaucoma is typically blind and painful requiring enucleation or intrascleral prosthesis.

Cataract

First cataract must be differentiated from the normal ageing change, lenticular (nuclear) sclerosis. Sclerosis occurs in all animals at middle age and is seen first in the dogs and cat at approximately 6 years of age. It is a change in central density and does not prevent a fundic examination or vision.

Cataract is defined as any opacity of the lens or its capsule. Cataracts are then divided by severity (incipient, immature, mature and hypermature), by location (capsular, cortical-anterior, posterior, equatorial, nuclear), by etiology (inherited, metabolic, traumatic, inflammatory, electric, nutritional, radiation, toxic) and by age of onset (congenital, juvenile, adult, senile). The most common reasons for cataracts in dogs are inherited and diabetes mellitus. It is important to know that all dogs with diabetes mellitus will get cataracts with >60% cataractous within a year of onset of diabetes. Of those dogs requiring surgery, diabetes may account for 30-50% of surgical cataracts.

The treatment of choice for progressive and vision impairing cataracts is phacoemulsification with intraocular lens implantation. The success of this technique is generally considered to be 90-95%. For those animals with a significant cataract that do not undergo lens removal, the veterinarian must monitor for lens-induced uveitis, retinal detachment and secondary glaucoma. Monitoring of IOP and treatment with topical NSAID’s is generally indicated. The lens may also luxate. This is most common in the terrier breeds and has been shown to be inherited in a simple autosomal recessive fashion. There is a DNA test for the terrier dogs for Primary Lens Luxation.
References


There are three pathological options of eye coloring. We can see:

- **Red eye** (corneal neovascularization, hyphaema) result from corneal inflammation or from retinal detachment, trauma, intraocular surgery, renal failure and hypertension.
- **Blue eye** (corneal edema, swelling, corneal overhydration) result from inhibition of fluid by the epithelium or stroma.
- **Black eye** (pigmentary keratitis).

Corneal pigmentation is most commonly associated with chronic inflammation. Corneal congenital melanosis or pigmentation occurs infrequently in dog. Pigmentary keratitis is not a diagnosis but is non specific response to chronic corneal irritation as seen with exposure. It can start due to brachycephalic ocular syndrome, lagophthalmos, chronic ulcerative dystrophy, facial nerve dysfunction, macropalpebral fissure, buphthalmus with chronic glaucoma, etc. Another cause is frictional irritation (distichiasis, trichiasis, ectopic cilia, nasal skin folds), tear film abnormalities (keratoconjunctivitis sicca), or chronic immunologic stimulation such CSK (chronic superficial keratoconjunctivitis).

All animals with “black eye” should undergo the following evaluation:

- STT – Schirmer tear test,
- Assessment of palpebral reflex,
- Fluorescein staining,
- Examination for presence of distichiasis, trichiasis and/or ectopic cilia,
- Assessment for entropion or ectropion,
- Corneal cytology in case of mass like lesion as seen with CSK,
- Tonometry.

For “black eye” preferred term is corneal melanosis, but it is frequently called corneal pimentation or pigmentary keratitis. Melanin is deposited in the corneal epithelium and sometimes the anterior corneal stroma and originates from proliferation and migration of normal limbal melanocytes during corneal inflammation. The more heavily melanotic the
limbus, the more likely and the denser the corneal melanosis. With severe and/or chronic irritation, melanosis is accompanied by changes in the corneal epithelium such as thickening, rete peg formation, metaplasia, vascularization and keratinization. Corneal pigmentation is a result of migration of the melanocytic cells from the limbal and perilimbal tissues. Melanin pigment is deposited in the basal epithelial cells and the superficial (anterior) stroma, and is found in macrophages and fibroblasts.

Corneal melanosis itself is not normally treated unless it is rapidly progressive in susceptible brachycephalic breeds or is interfering with vision. Detection of pigmentary keratitis should always stimulate thorough diagnostic investigation for underlying source of irritation. The underlying cause should be removed if possible. It is possible in dogs with CSK, removal of source of frictional irritation, reconstructive eyelid surgery, removal of abnormal lashes and aberrant dermis, possible partial removal of nasal folds and tear replacement therapy.

Radical therapy is surgical removal of nontransparent anterior cornea but it has been suggested if initial causes have been corrected. The specific procedure for this method is superficial lamellar keratectomy. Superficial keratectomy is most commonly performed using traditional surgical instruments and under magnification. However, frequent recurrence of pigment and corneal scarring, despite appropriate therapy, generally limits success of this procedure. Application of strontium 90, beta radiation therapy or cryotherapy has also been suggested, but success rate is unknown. Topical cyclosporine, corticosteroids, tacrolimus are frequently used in treatment of pigmentary keratitis. The efficacy of these treatments is unknown, although studies have demonstrated effectiveness in treatment of inflammatory disease of the canine cornea and its associated corneal pigmentation. Radical way of improving of vision is total keratoplasty using donor cornea or substitute.

Another less common source of corneal pigmentation is anterior synechiae and the adherence of anterior uveal cysts to the cornea. Cysts of the anterior uvea may be either congenital or acquired (as the result of uveal inflammation or degeneration). The pigmented cells may arise from the pigmented epithelium of the ciliary body, iridal stroma, and posterior iridal epithelium. These cyst can be large and attach to the corneal epithelium, or the can rupture and liberate pigment that adheres to the posterior aspect of the cornea.

Species variations in the tendency for development of pigmentary keratitis exist, birds are extremely resistant, horses and cats are moderately resistant and dogs are extremely susceptible. The reason is unknown.

Prognosis – the aim of surgery is not only to halt the progression of the corneal pigmentation but also to reduce the extent and density of existing pigment to improve corneal clarity and transparency. The prognosis is good with early and accurate diagnosis and prompt surgical management. Although medical and surgical treatment can help dogs with advanced disease, the beneficial effects are more likely to be seen in the overall ocular surface health rather than in significantly improved vision.